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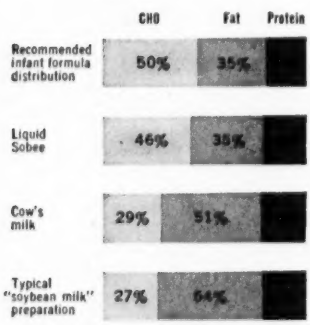

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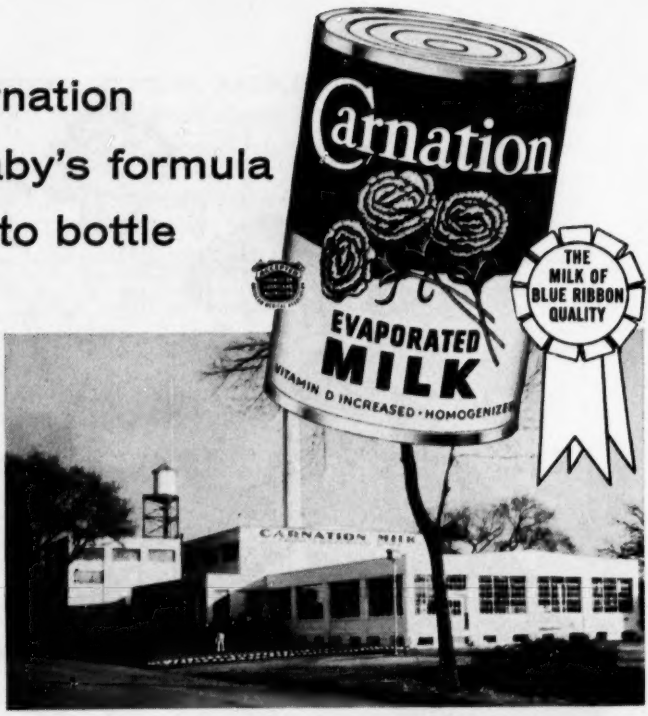

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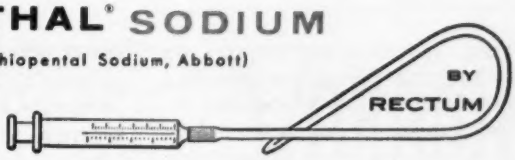

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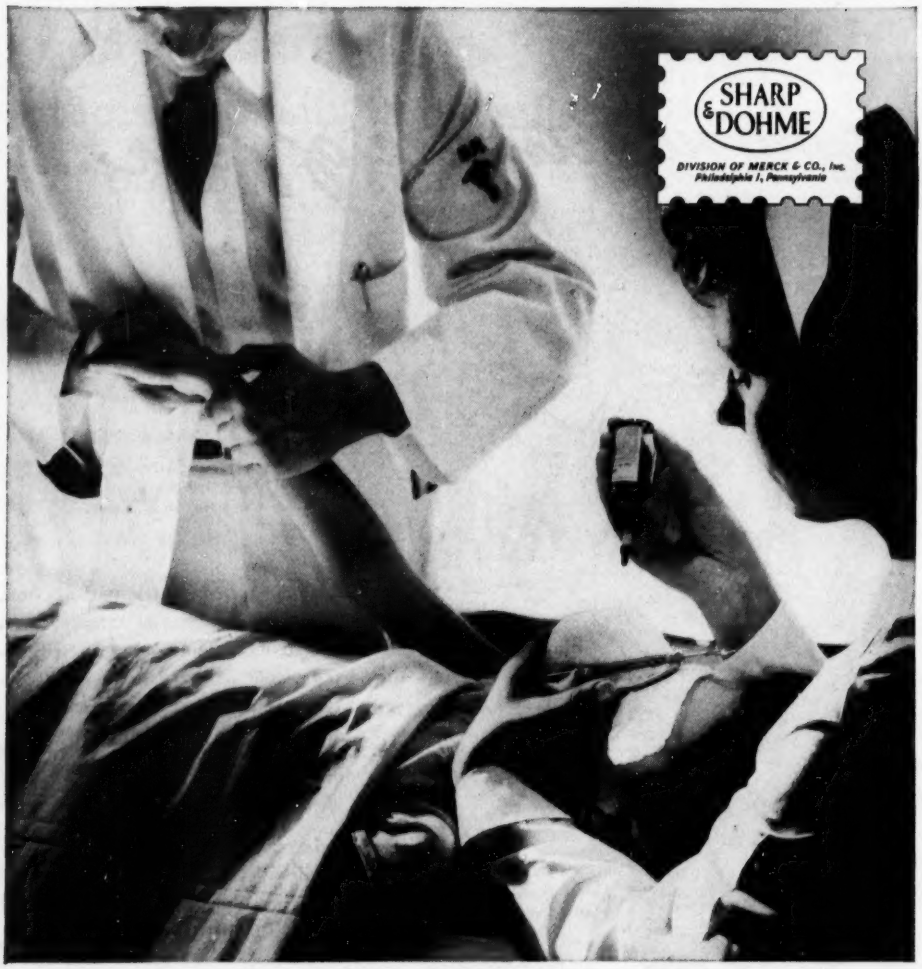

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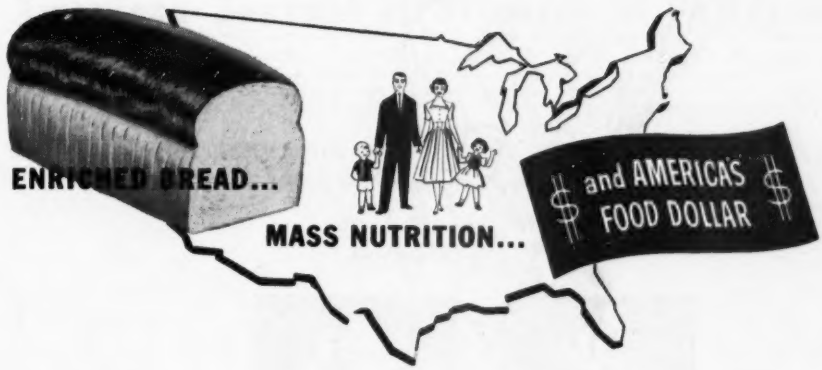

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1. Bureau of Labor Statistics, United States Department of Labor, Jan., 1954.
2. Sebrell, W.H.: Trends and Needs in Nutrition, J.A.M.A. *152:*42 (May 2) 1953.
3. Council on Foods and Nutrition, American Medical Association: A Statement of General Policy Concerning the Addition of Specific Nutrients to Foods, J.A.M.A. *154:*145 (Jan. 9) 1954.
4. Shank, R.E.: Revisions of the Recommended Dietary Allowances, J. Am. Dietet. A. *30:*105 (Feb.) 1954.
5. Sherman, H.C.: Chemistry of Food and Nutrition, ed. 8, New York, The Macmillan Co., 1952, pp. 212, 599.

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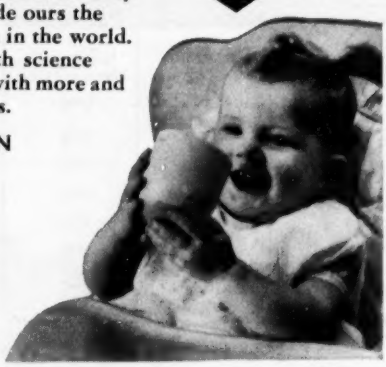

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PAIN ASSOCIATED WITH ACUTE POLIOMYELITIS

Neurologic and Therapeutic Considerations

PER BENDZ, M.D.
BROMMA, SWEDEN

PAIN IS a conspicuous symptom in acute poliomyelitis. Besides headache, pain occurs in the trunk and extremities, usually in two episodes during the course of the disease: initially, before motor damage has developed, and later, in the subacute stage, when progression of the disease has more or less ceased and paralysis is present. We might accordingly speak of preparalytic and postparalytic pain. Even though the pain usually abates during the development of paralysis itself, it may, nevertheless, persist continuously. It may be absent during one phase—commonly, the initial one—but seldom during both.

The pain is partly spontaneous, in the form of aching, and partly provoked, in the form of tenderness. The aching is both continuous and paroxysmal. The continuous form is felt as an intense irritating pain, mostly resembling postexercise ache or neuralgia. The paroxysmal form consists of brief darting pains, for example, in an extremity as far as the hands and feet. These pains are common in the cranial region too; in the thorax they are felt as stitch-like pains, and in the abdominal region they simulate acute surgical affections. The intense pain gives rise to a marked need of movement, which in the preparalytic stage produces motor restlessness and in the postparalytic stage is invariably a troublesome problem in management of the patient.

THEORIES ON THE PATHOGENESIS OF POLIOMYELITIS PAIN

Since the pain in the trunk and extremities is often a troublesome factor and predisposes to contractures, it presents certain therapeutic problems. It is, moreover, of some theoretical interest, and there has been considerable speculation as to its pathogenesis.

Guyton and Reeder,[1] for instance, on the basis of experimental rhizotomy in animals, consider that the pain is caused by direct irritation of the neuromuscular spindles due to products of atrophy. Other authors (including Smith, Graubard, and Rosenblatt) attribute the pain to peripheral angiospasm and ischemia and refer to good therapeutic results by the use of, e. g., vasodilators.* Many believe that there is a causal relationship between muscular spasm and the pain, and Kenny's treatment is based on this view.[5] The theories of a neurogenous origin are founded on histopathologic findings in various sensory neurons from spinal ganglia and the sites of entry of the dorsal roots in the region of Clarke's column and up to the thalamic centers.†

From the Stockholm Hospital for Infectious Diseases.

* References 2-4.

† References 6 and 7.

The role of the sympathetic nervous system has also been discussed.‡ I have conducted an investigation with Lewis's circulation test on 50 poliomyelitis patients in the subacute phase of pain and have been able, like the Danes, Lundbaek and Skinhøj,§ to demonstrate a transient dysfunction of the peripheral circulation. There was no demonstrable correlation, however, between this dysfunction and pain. Incidentally, it is known that pain, whatever its origin, is often attended by symptoms of increased sympathetic tone, e. g., in the vasomotor system.

In seeking to elucidate the cause of a pain, the first step must be to localize the stimulus factor, i. e., the source of the pain. In so doing, the clinical localization of pain and tenderness should be determined first.

As regards the pains associated with poliomyelitis, the first question that arises is, are they generalized, or do they follow a circumscribed logical system?

PERSONAL INVESTIGATIONS

Since the autumn of 1947, I have investigated with respect to pain about 200 cases of poliomyelitis with paralysis of the extremities. It may be observed that a close correlation exists between the pain and the motor lesions. Of the cases with paralysis of the legs, pain in the legs occurred in 95% in the preparalytic stage and in 85% in the postparalytic phase. The corresponding figures for cases with paralysis of the arms were 75% and 35%, respectively, having pain and tenderness in the upper extremities. Only in exceptional instances did pain occur in nonparalytic extremities. If either the legs or the arms were paralytic, they alone had pain. If the degree of paralysis varied in a pair of extremities, the pain was greatest in the one affected most severely. Curiously enough, there was no pain in cases with distal paralysis alone, i. e., paralysis of the hands and feet, which is somewhat uncommon. The pain, it would seem, is confined to cases with paralysis of proximal muscle groups.

Cases clinically assignable to the etiologically heterogeneous group consisting of nonparalytic poliomyelitis seldom if ever show pain in the extremities.

As regards pain in the lumbar region alone, it is not specific for poliomyelitis but is equally common in various other virus infections with or without complications in the central nervous system.

The continuous pain has the same character in both the preparalytic and the postparalytic stage. During the initial phase of intense pain in the postparalytic stage, the pain is felt to come from the proximal parts of the extremities and to radiate towards the hands or feet. So far as the upper extremities are concerned, a pain center may thus be localized over the scapula and in the supraclavicular fossa, the pain radiating down to the elbow. As regards the lower extremities, the sacral region and the gluteal region at the crista iliaca and lateral thereto over the gluteus medius and minimus muscles constitute a similar pain center, with radiation down to the region of the knee. In the later stages of the period of pain, the pain center usually moves distally, i. e., around the elbow, with pain in the proximal part of the forearm, or to the region of the knee, with radiation laterally down the lower leg.

‡ References 8 and 9.

§ References 10 and 11.

The paroxysmal differs from the continuous pain in that it radiates to the hands and feet and is commonest during the initial phase of intense pain, though it may be predominant in pain of long duration.

Active movements provoke both the dull and the paroxysmal pain, and since the pain gives rise to a pronounced need of movement, a vicious circle often results. Patients with total paralysis of the extremities usually experience little pain, perhaps because they lie still.

Tenderness provoked by movements and palpation coexists with the postparalytic pain, but persists longer.

Analysis of the localization of this tenderness shows that it is not confined to certain soft tissues or uniformly distributed over an extremity. It is greatest, and indeed sometimes present only, over nerve and vessel trunks where they are palpable, and is next greatest over certain muscular regions. In paralysis of the arms, for instance, there is constant tenderness over the brachial plexus and the palpable nerve and vessel trunks of the upper arm down to the cubital fossa. In paralysis of the legs, there is pronounced tenderness over the ischiadic nerve, from the proximal point where it emerges from the sacrum along the whole course to the popliteal fossa and branches in the tibial or peroneal nerve. Maximum tenderness is constantly found proximally in the thigh, over the fossa ovalis with its palpable vessel and nerve trunks.

Tenderness in the popliteal fossa and in the calf when pressure is applied on the midline is equally pronounced, as in cases of sciatica of varying pathogenesis, notably in a herniated disc. Moreover, the Lasègue test usually is strongly positive, with a maximum painless range of extension of 30 degrees.

Muscular tenderness is not confined to the paralytic muscles per se, but to certain paralytic muscular regions. It mainly affects proximal muscular regions: the muscles of the shoulder girdle (the supra- and infraspinatus, teres, pectoralis, and serratus); those of the pelvic girdle (the gluteus muscles—notably, the gluteus medius proximally at the crista iliaca—and the muscles proximally in the thigh, the tensor fasciae latae and rectus femoris, and, especially the adductors). A comparison might be made here with the fourth lumbar syndrome in herniated disc.

Worthy of note is the fact that the muscular tenderness markedly subsides distad, being only very slight or quite absent below the elbows and knees. In this respect, too, the symptoms are consistent with those in compression of the roots due to a herniated disc.

Muscular extension pain occurs in paralytic muscles that have contracted; this applies to flexor muscles, such as the biceps brachii or the semiflexores femoris, but also, for example, to the triceps surae. Muscles paralyzed by poliomyelitis, or their more powerful antagonists, readily become contracted, this being partly due to increased muscular irritability. This muscle extension pain does not differ in principle from that of normal muscles in a state of contracture, for instance, following surgical fixation or conditions attended by transient pain in a joint.

RESULTS

The foregoing clinical analysis of the pains associated with acute poliomyelitis thus shows that they have both a neuralgic and a myalgic element. The neuralgia, both continuous and paroxysmal, with its segmental distribution, and the myalgic

tenderness, with its segmental localization, clearly suggest that the source of pain is to be sought in those nerve roots—both dorsal and ventral—that arise from the segments of spinal cord affected.

COMMENT

Parallels can be drawn with the symptoms of pain in acute infectious polyradiculitis, both in the acute and the subacute phase. This applies to those cases in which sensory loss is either inappreciable or absent from the outset or regresses more rapidly than the symptoms of motor loss. The pain in that disease is identical with that in acute poliomyelitis, i. e., neuralgic and myalgic. The occurrence of pain in polyradiculitis presupposes intact pain condition in the dorsal roots.

Corresponding parallels can also be drawn with mechanical lesions of the roots, notably, a herniated disc. The pains originating from lesions of the dorsal roots both in the cervical and in the lumbar regions, as described in detail by several authors, are well known.‖ Perhaps less well known are those which emanate from the ventral roots. As early an investigator as Magendie experimentally produced pain in animals by irritation of the peripheral portion of a severed ventral root.[14] Several other authors have verified his observation; and most recently Frykholm, in his dissertation of 1951, studied pain phenomena arising from cervical ventral roots in a herniated disc.[15] The pain originating from the ventral roots is chiefly myalgic and occurs in proximal parts of the extremities, such as the scapular, trapezius, pectoral, and axillary regions, as well as in the gluteal region and the proximal muscles of the thigh. The explanations of these myalgic symptoms which have been given are manifold and hypothetical, but will not be discussed in detail here.

The neuralgic element of poliomyelitis pain seems to be referable to the dorsal roots, and the myalgic, to the ventral roots. That the myalgic symptoms persist longer than the neuralgic is due to involvement mainly of the motor portion.

It is difficult to say, other than hypothetically, the cause of this radiculosis of both dorsal and ventral roots. It is known, for instance, from experimental research on poliomyelitis (Sabin and Bodian and others), that in the acute stage the virus multiples not only in the nerve cells themselves but in the whole of the peripheral motor neuron. Further, the virus is known to attack also dorsal parts of the grey matter of the spinal cord, as well as spinal ganglia.[16] In the subacute stage, regenerative and proliferative processes occur in and around the nerve roots. The radicular process is probably confined largely to the meningeal portion of the radices, i. e., it is a meningoradiculosis. Variations in severity, character, and distribution of the dorsal and ventral root involvement serve to explain individual variations in the clinical manifestations of the pain.

I have not investigated the protein content of the cerebrospinal fluid after the acute stage. However, investigations of this kind were reported by the German workers, Neumann,[17] Walther, Schäfer,[18] and Stier,[19] in 1949 and 1950. Stier correlated the protein content of the cerebrospinal fluid with the prognosis for the restitution of paralysis; Neumann, for his part, with the pain, though only in respect of certain cases with intense and protracted pain of neuralgic type. The pain was attributed to radiculitis of the dorsal roots, as well as to ganglionitis.

‖ References 12 and 13.

THERAPEUTIC PROBLEMS

Local Methods.—That measures to alleviate the pain can only be symptomatic is evident from the above conclusions on its genesis. We can distinguish between local and general measures. Of the former, reference has already been made to various hyperemizing measures, such as hot baths or packs. It is a well-known fact that effective hyperemia in painful parts of the body has a favorable influence on the pain. For instance, the pain in poliomyelitis can be readily alleviated by hyperemizing a painful area by means of friction heat (for example, by massaging the skin with petrolatum) or by utilizing the reactive hyperemia that develops after an extremity has been deprived of its blood supply for a few minutes (with a blood

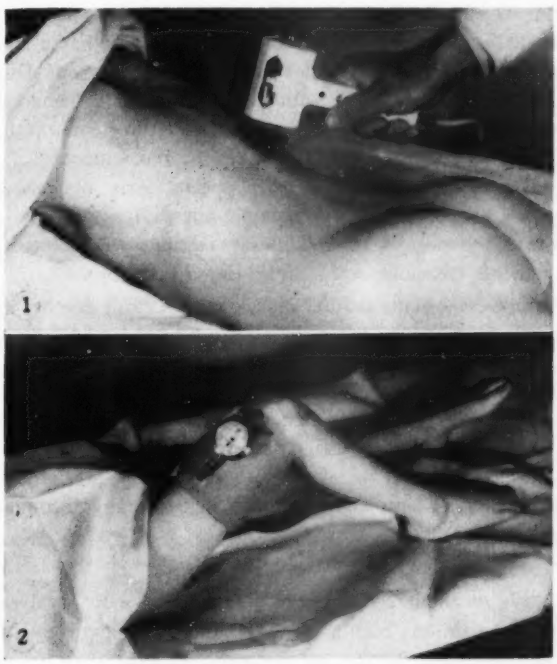

Fig. 1.—Machine for vibration massage.
Fig. 2.—Blood pressure cuff for arterial stasis.

pressure cuff). Repeated experiments have shown that the alleviation of pain commences with the reactive phase. Venous stasis does not have the same effect.

American workers, in particular, have used vasodilators for purposes of hyperemization as a substitute for hot packs.[4] The analgesic effect is dependent on the effectiveness of the hyperemia; hence, fairly large doses have been required. Both positive and decidedly negative results have been reported by various authors.¶ Benzazoline (Priscoline) has chiefly been used, since it has a good and reliable vasodilatory effect. I have had inconsistent results with regard to the analgesic effect of, for instance, benzazoline; the large doses required—100 mg. and over

¶ References 2 and 20.

every four hours—often produce side-effects greater than the pain itself. Even though a very good peripheral circulation can be obtained with benzazoline in small doses, pain is not affected to the same degree. Benzazoline should be used to improve poor peripheral circulation, i. e., in cold hands and feet, a common symptom in acute poliomyelitis. For analgesic purposes, however, it is inadequate.

Another simple method consists of local anesthesia subcutaneously where pain or tenderness appears to be maximal. This treatment largely affects the radiating pain, which is the most irritating. It can be used to advantage in the case of pain in the lumbar region or, by and large, in circumscribed areas of pain.

General Methods.—Drugs with a general action are various analgesics and sedatives. It is important to use agents combining effectiveness with relative innocuousness. Caffeine is such a drug, either in pure form or as coffee. Its analgesic effect in poliomyelitis is exceptionally good.# Moreover, it has a specific sedative action in encephalitis. At the Stockholm Hospital for Infectious Diseases, coffee, pure caffeine, or caffeine combined with acetophenetidin (Phenacetin) has been routinely used against poliomyelitis pains for at least 15 years, both in the acute and the subacute phases of the disease, and can be recommended.

The tenderness is best influenced by a special form of massage, vibration massage. For this purpose, there are simple massaging machines that vibrate according to the alternating current. This is a simple and effective method that can be substituted for laborious wrappings (Fig. 1).

Muscle Contracture.—Acute painful muscle contractures due to "muscle spasm" in the elbows, knees, or ankles (drop foot) can be resolved by a simple method. The aim is to utilize that alleviation of pain which is obtained in the reactive hyperemia phase after a few minutes of arterial stasis. A blood pressure cuff, fitted proximal to the elbow or knee, is inflated to a pressure of 150 to 200 mm. of Hg, and after one to two minutes of stasis the pressure is removed. After 15 to 20 seconds, the pain subsides, and the arm or leg can then be straightened out or the drop foot corrected. This simple method can be especially recommended in the case of children (Fig. 2).

SUMMARY

Clinical analysis of about 200 cases of poliomyelitis with paralysis of extremities showed that the pain has both a neuralgic and a myalgic element.

The character and distribution of the pain coincide with the symptoms in common root affections, such as herniated disc and acute polyradiculitis.

Poliomyelitis pain, it is accordingly asserted, generally has a radicular genesis, the neuralgic element being referable to the dorsal roots and the myalgic to the ventral roots.

The therapy is symptomatic, and I advocate caffeine, in particular, as an adequate drug to relieve the neuralgic pain and various local measures, such as local hyperemia or anesthesia, as well as vibration massage, to alleviate the myalgic pain.

For the treatment of acute painful muscle contractures (muscle spasm), I recommend a simple method consisting in the production of reactive hyperemia after brief arterial stasis by means of a blood pressure cuff, which treatment brings about immediate freedom from pain for muscle extension.

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ISONIAZID IN TREATMENT OF TUBERCULOSIS IN CHILDHOOD

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THE ADVENT of streptomycin as a therapeutic agent in tuberculosis has caused considerable modification of the previously hopeless prognosis which attended the diagnosis of tuberculous meningitis in children. As pointed out in a recent study,[1] however, the results of treatment with this drug in conjunction with either thiazolsulfone (Promizole) or paraaminosalicylic acid have been far short of the desired goal. Further, there has remained this ever-present question: When should one use streptomycin in the treatment of the lesser forms of tuberculosis in childhood?

Since there are many questions not completely answered and since isoniazid has been demonstrated to be a promising tuberculostatic compound, it has seemed advisable to continue the clinical use of this agent in the treatment of the various forms of tuberculosis as the disease appears in children. The Committee on Chemotherapy and Antibiotics of the American College of Chest Physicians[2] feels that "isoniazid has not yet been used extensively enough in children for definite evaluation" of effectiveness of therapy of tuberculosis in that age group. That this present study is incomplete is apparent. However, it may give some indication of the value of this newest tuberculosis therapeutic adjuvant.

TUBERCULOUS MENINGITIS

Eleven patients with tuberculous meningitis were treated with isoniazid,* in combination with other chemotherapeutic agents (Table 1). Seven of these patients have survived for a period ranging from 3 to 15 months following the institution of therapy.†

While nine patients in this group also received streptomycin by the intrathecal route, there has been a tendency to forego this therapeutic approach. Of the last four patients treated, only two received intrathecal injections of streptomycin, and they received only 14 and 5 injections, respectively.

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* The isoniazid (Rimifon) used in this study was furnished by Hoffman-LaRoche Inc., Nutley, N. J.

† All statistics are as of Nov. 15, 1953.

TABLE 1.—*Treatment of Tuberculous Meningitis*

Patient	Age	Race	Sex	Duration of Symptoms, Days	Streptomycin		Isoniazid, Days	Other Therapy	X-Ray Diagnosis, Type of Tbc.	Relapse	Results
					I. M., Days	I. T., Days					
C. S.	5 yr.	N	M	5	63	41	293	PAS	Miliary	—	Mild quadriplegia; asymptomatic 15 mo.
S. S.	2 yr.	W	F	10	109	14	171	PAS	Mediastinal	—	Home; well 11½ mo.
R. J.	12 mo.	N	M	30	300	92	54 (terminal)	PAS thiazol-sulphone (Promizole)	Mediastinal	Yes	Died, 15 mo. 3 days
G. T.	23 mo.	N	M	90 (no meningeal symptoms)	125	..	272	PAS	Miliary	—	Apparently well 15 mo.
L. G.	10 mo.	N	M	5	290	40	280	PAS	Mediastinal	—	Hydrocephalus, apparently arrested
T. J.	6 yr.	N	M	21	180	60	Yes	PPD PAS	Miliary	—	Died, 254 days; skull fracture during manic spell
C. G.	2½ yr.	N	M	14	20	17	Yes	PAS	Mediastinal	—	Died, 20 days
V. W.	16 mo.	N	F	10	30	14	28	PAS	Miliary	—	Downhill course; died in coma 30 days after admission
J. C.	8 yr.	W	M	6	99 (2 inj/wk. last 5 wk.)	5	99	PAS	Mediastinal	—	Apparently well for 3 mo.; has arrested hydrocephalus (congenital) with encephalocele
M. J.	27 mo.	N	F	6	189 (2 inj/wk. last 2 wk.)	None	189	PAS	Miliary	—	Well, 6½ mo.
N. B.	21 mo.	W	M	6	105	None	117	PAS	Mediastinal	—	Spastic diplegia (arms), 3 mo. after admission

Our present therapeutic combination consists of intramuscular injections of streptomycin, 40 to 80 mg. per kilogram of body weight per day (with maximum daily dosage of 1 gm.), paraaminosalicylic acid, 0.15 gm. per kilogram of body weight per day, and isoniazid, 6 to 8 mg. per kilogram of body weight per day (earlier patients received 4 mg.). This constituted the dosage of these drugs whenever used in the treatment of tuberculous disease mentioned in this paper, unless otherwise noted.

PRIMARY PULMONARY TUBERCULOSIS

While it is generally recognized that primary tuberculous disease most frequently resolves without serious sequelae, practically all the cases treated here exhibited features which seemed to indicate the advisability of therapy (Table 2). For example, there were only four cases of uncomplicated mediastinal tuberculosis.

TABLE 2.—*Treatment of Primary Pulmonary Tuberculosis*

Name	Age	Race	Sex	Diagnosis	Duration of Isoniazid Therapy, Mo.	Result
J. C.	4 yr.	N	F	Mediastinal tbc	3	Healed
B. C.	20 mo.	W	M	Mediastinal tbc	4	Healed
B. C.	6 mo.	W	F	Mediastinal tbc	4½	Healed
L. K.	3 wk.	N	F	Mediastinal tbc	11, plus streptomycin, 1	Healed
E. M.	3 yr.	N	F	Tbc pneumonia	6	Cleared
S. J.	11 mo.	N	F	Tbc pneumonia	4	Cleared
C. S.	5 yr.	N	M	Mediastinal tbc; Atelectasis	4	Healed
J. R.	22 mo.	N	M	Mediastinal tbc; Atelectasis	3	Healed
L. D.	12 mo.	N	F	Mediastinal tbc; Tbc mastoiditis	6	Healed
C. P.	8 mo.	W	M	Pulmonary tbc; Tbc rt. ankle	17, plus streptomycin, 12	Healed

Two of these occurred in infants under 6 months of age (Fig. 1), one of them being a 23-day-old Negro girl (L. K.).[3] That the disease process was active in these two instances seems unquestionable in view of the age of the patients and the serial x-ray follow-up. In the other two patients, the disease was felt to be in an active state because of the appearance of the chest x-ray and the presence of low-grade fever and an elevated erythrocyte sedimentation rate. Recovery was satisfactorily prompt in each instance.

Two Negro boys, 22 months (J. R.) and 5 years (C. S.) of age (Fig. 2), respectively, exhibited atelectasis in addition to mediastinal tuberculosis, and two others, a 3-year-old Negro girl (E. M.) and an 11-month-old Negro girl (S. J.) (Fig. 3), had tuberculous pneumonia. In each instance, recovery was uneventful. A one-year-old Negro patient (L. D.) had tuberculous mastoiditis in addition to x-ray changes indicative of mediastinal tuberculosis. She received isoniazid for six months following mastoidectomy, and there has been no further demonstrable activity of the tuberculous process, either in the mastoid region or in the lung fields.

The other patient (C. P.) (Fig. 4) had widespread pulmonary tuberculosis. At 3 months of age, he developed a severe cough and anorexia and from that time

on failed to gain weight satisfactorily. He was seen by his family physician, and the first chest x-ray was taken. In spite of the readily demonstrable lung pathology in this and in a second x-ray, taken four days later, no tuberculin test was done until a third chest x-day was taken (four months after onset of symptoms). When the tuberculin test was found to be positive, the patient was 8 months of age and weighed only 6,000 gm. Cough was still severe, and anorexia persisted. The patient was given streptomycin intramuscularly, and a month later isoniazid was added

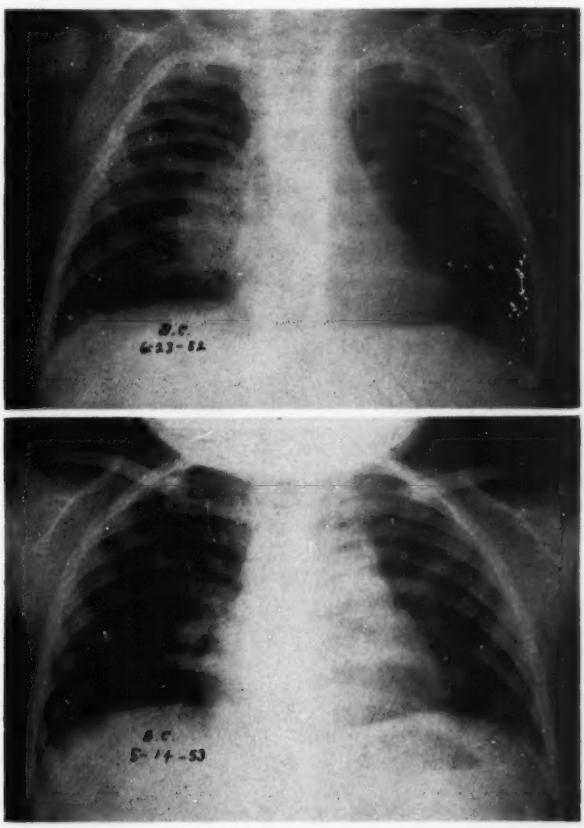

Fig. 1.—Uncomplicated mediastinal tuberculosis in two infants under 6 months of age.

to the regimen. One week after this, the right ankle became swollen and tender. A tentative diagnosis of tuberculosis of the ankle was made, and the patient was referred for orthopedic care. Isoniazid and streptomycin were continued for three and four months, respectively, before the patient was admitted to Crippled Children's Hospital for care of his ankle. At the time of writing this paper, he has received isoniazid for 17 months, and was given streptomycin twice weekly for a 12-month period. The patient appears well and healthy, and an x-ray of the chest shows almost complete healing of the disease process. The ankle shows no disease activity.

TUBERCULOUS ADENITIS

Two patients with tuberculous cervical adenitis received isoniazid therapy. One 3-year-old Negro boy received the drug for three months immediately after excision of the node but received no preoperative therapy. He has been well since operation. The other patient, a 2-year-old white girl, received both isoniazid and streptomycin for seven weeks prior to excision of the node. Streptomycin was given daily for two weeks and twice weekly thereafter. Preoperative therapy seemed to have little

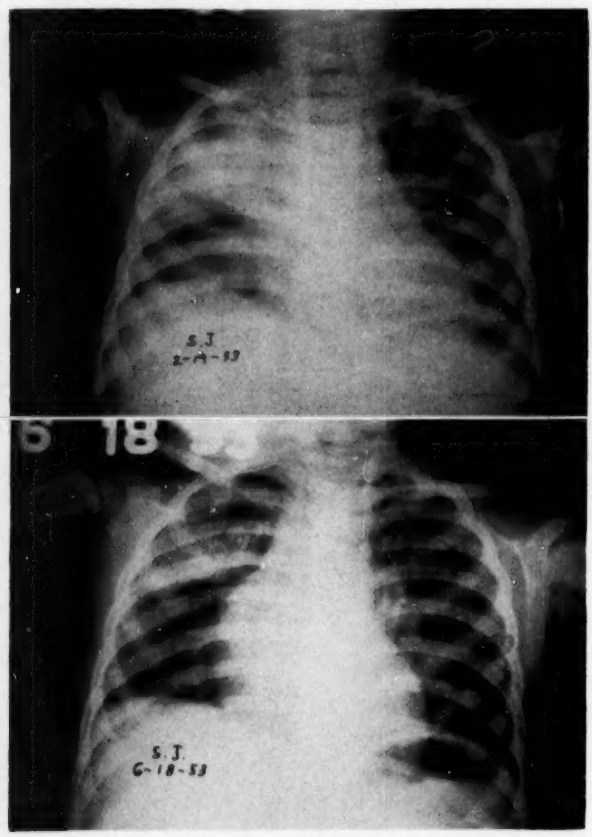

Fig. 2.—Atelectasis in addition to mediastinal tuberculosis in two Negro boys, 22 months and 5 years of age, respectively.

beneficial effect on the node. After surgical excision, the patient received isoniazid for five weeks and streptomycin twice weekly for one month. She has apparently been well for the past year.

TUBERCULOUS PLEURISY WITH EFFUSION

A 9-year-old Negro girl had pleurisy with effusion (Fig. 5). She received isoniazid for a period of two months. The effusion persisted for four months, and isoniazid seemed to have little influence on the course of the disease.

TOXIC REACTIONS

All patients treated with isoniazid exhibited euphoria. The atmosphere of the tuberculosis ward changed from one of black despair to one of cheerfulness and gaiety.

Only one manic disturbance occurred, but this one lead to a fatal outcome. This patient (T. J.),[1] a 6-year-old Negro boy with tuberculous meningitis, had received isoniazid (4 mg. per kilogram of body weight per day) for one month when the

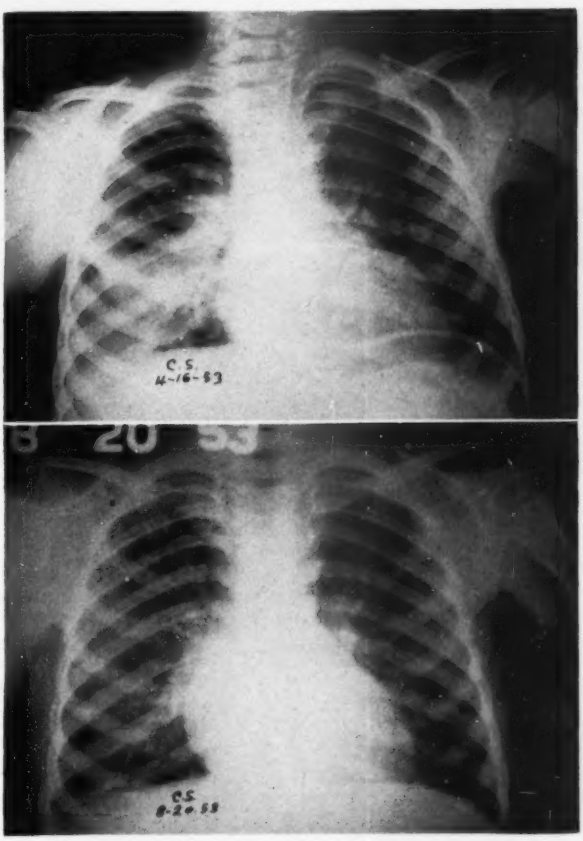

Fig. 3.—Atelectasis in addition to mediastinal tuberculosis in two Negro girls, 3 years and 11 months of age, respectively.

disturbance occurred. In retrospect, it may be said that he had begun to be somewhat manic for the preceding 36 hours, but on this day he suddenly leaped from the bed and ran into a closed door. He fell to the floor, arose, and ran into the wall, again knocking himself to the floor. He was then returned to bed and threshed wildly about until sedation was given.

From that time on he lay in semicoma. He could not see, hear, or speak. An x-ray of the skull revealed a linear fracture, 11 cm. in length, near the midline in the occipital area (Fig. 6).

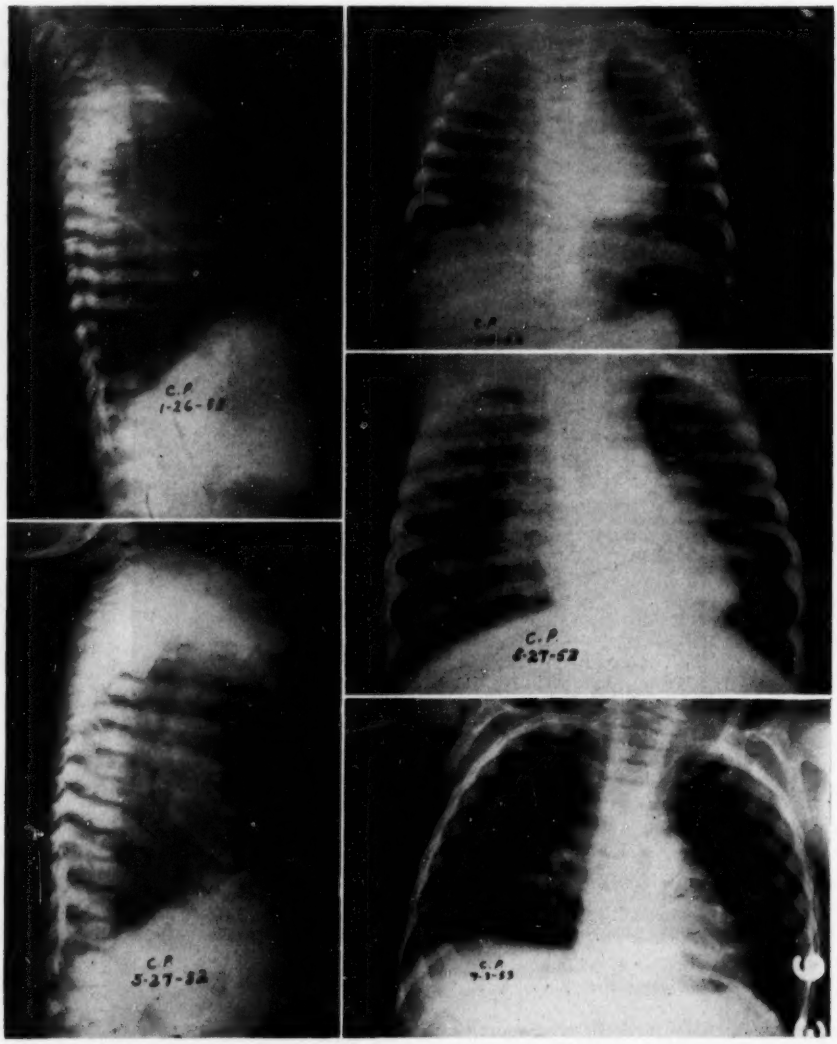

Fig. 4.—Widespread pulmonary tuberculosis in infant C. P.

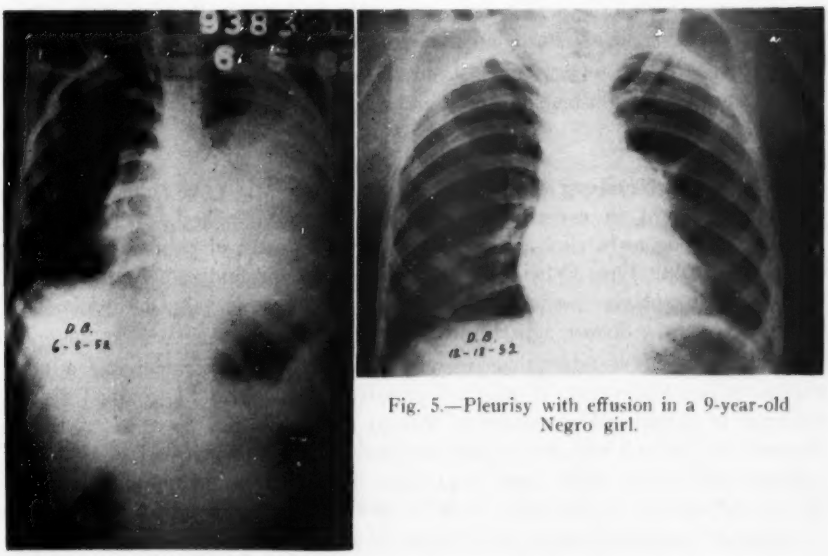

Fig. 5.—Pleurisy with effusion in a 9-year-old Negro girl.

Fig. 6.—X-ray of skull of 6-year-old Negro boy with tuberculous meningitis, showing linear fracture near midline in occipital area.

After several weeks, there was partial return of the auditory function, and later the patient was able to speak a few words. He appeared to be completely blind until his death, eight months after admission to the hospital.

No other side-effects were noted. Anemia of moderate degree was often present, but no more than might be expected from any group of chronically ill infants.

COMMENT

The work of Grunberg and Schnitzer [4] proved isoniazid to be an effective antituberculosis agent in experimental disease. Robitzek, Selikoff, and Ornstein [5] showed the drug to be clinically effective in the treatment of pulmonary tuberculosis of the adult type. Others have substantiated their finding.‡ In the present study, an attempt was made to determine the therapeutic value of isoniazid in tuberculosis as the disease appears in children.

The treatment of tuberculous meningitis in children has undergone a great change at our institution. Waddell's [9] experience has led to the gradual discontinuance of intrathecal streptomycin therapy. Isoniazid has been added to the armamentarium, and with the regimen outlined earlier in this paper 7 of 11 treated patients (63%) are living more than three months after institution of therapy. Before the addition of isoniazid, 14 of 33 treated patients survived (42%).

Ratner [10] has suggested the use of isoniazid alone in the treatment of tuberculous meningitis. Since Steenken [11] and his associates have demonstrated the tendency toward development of drug-resistant organisms when isoniazid is used alone, this suggestion seems unwise. However, while there is little doubt as to the advisability of using all effective therapeutic agents in the treatment of tuberculous meningitis, distinct difference of opinion still exists as to the proper use of chemotherapeutic agents in the treatment of the lesser forms of tuberculous disease in children. Before the advent of isoniazid, one hesitated to use streptomycin in the treatment of a tuberculous diesase such as mediastinal tuberculosis unless the process appeared to be progressive. Use of that drug was largely reserved for miliary tuberculosis and tuberculous meningitis.

Waring [12] has advocated chemotherapy in patients who develop a positive reaction to the tuberculin test, even though there is no x-ray or clinical evidence of disease. If one subscribes to the endogenous theory of causation of all tuberculosis of the adult type, such an approach may be especially logical. However, even then there is a question whether or not a course of therapy with streptomycin and/or isoniazid at this time would eradicate the tuberculous infection.

In the American literature, there seems to be no study concerned with the use of isoniazid in the treatment of the various forms of pulmonary tuberculosis in children. However, Filla and Savastano [13] cited several "partially contradictory" studies and, in their own study, concluded that isoniazid is no more effective on the primary foci than streptomycin and paraaminosalicylic acid. They pointed out that isoniazid has the advantage of minimal toxicity and remarkable effect on the general condition of the patient.

In this study, isoniazid was used alone, and results were satisfactory in cases of mediastinal tuberculosis, mediastinal tuberculosis with atelectasis, and tubercu-

‡ References 6, 7, and 8.

lous pneumonia. One case of pulmonary tuberculosis was treated with isoniazid and streptomycin, with relatively prompt recovery. The agent seemed to have little effect on tuberculous adenitis and in one case on pleurisy with effusion. In conjunction with streptomycin, improved results in the therapy of tuberculous meningitis were obtained.

SUMMARY

Isoniazid was used in the treatment of the various forms of tuberculosis as the disease appears in childhood. It appears to be effective in the therapy of mediastinal tuberculosis, mediastinal tuberculosis with atelectasis, tuberculous pneumonia, and (in conjunction with streptomycin) pulmonary tuberculosis. Tuberculous adenitis and one case of pleurisy with effusion did not appear to be influenced by the drug. In conjunction with streptomycin, improved results in the treatment of tuberculous meningitis were obtained.

Mrs. Nellie Gentry gave technical assistance.

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ABO HETEROSPECIFIC PREGNANCY AND HEMOLYTIC DISEASE

A Study of Normal and Pathologic Variants

I. Patterns of Maternal A and B Isoantibodies in Unselected Pregnancies

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INCOMPATIBILITY of mother and child with respect to the blood groups AB and O is a common occurrence. Depending on the incidence of the genes for A, B, and O in a given population, approximately 20 to 25% of all pregnancies are heterospecific in the sense that the fetal red corpuscles possess an agglutinogen, A or B, not present in the mother, while the maternal serum contains the corresponding agglutinin, which is antagonistic to the fetal blood group. It is clear that the fetus ordinarily must be protected against the potentially harmful effects of the maternal isoantibodies. The mechanisms responsible for this protection are not well understood. By the same token, the nature of the process through which the fetus and the newborn infant may suffer damage in some instances of heterospecific pregnancy is not clear. There is unanimous agreement, however, that incompatibility of mother and fetus can produce a pathologic condition in the newborn. The criteria for the recognition of so-called ABO hemolytic disease have been slow in forthcoming, and it has been difficult to draw the line between the range of normal variants and disease. In part, these difficulties have been due to the use of different methods by different investigators and, particularly, to the scarcity of comparable studies made on normal or unselected control cases.

An obstacle which further delayed the acceptance of ABO heterospecific pregnancy as the cause of a hemolytic syndrome in the offspring was the usual failure of the direct Coombs's test to demonstrate coating of the fetal erythrocytes with maternal anti-A or anti-B antibody. This test had become the keystone of the modern theory of hemolytic disease by furnishing proof of the coating of fetal red cells with Rh antibody and had been found applicable to antigen-antibody reactions involving other red-cell antigens. The failure of the direct Coombs's test in most of the reported cases of ABO hemolytic disease not only created a theoretical problem but left the practicing physician and the clinical investigator without a simple and reliable tool for screening and diagnosis. In contrast to Rh

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antibodies which are always pathologic, the finding of agglutinins against A or B in the maternal serum was in itself without diagnostic significance, since they were present by definition in every heterospecific pregnancy. The height of the maternal agglutinin titer proved to be an unsatisfactory criterion. The characterization of anti-A and anti-B antibodies with special "immune" characteristics in the maternal serum was more promising. It was not clear in the beginning, however, how well the presence of immune anti-A or anti-B could be correlated with clinical manifestations in the infant. The various tests designed to demonstrate immune anti-A and anti-B, moreover, frequently gave divergent results and were somewhat cumbersome for rapid diagnosis.

With these considerations in mind, we thought it desirable to study the natural history of ABO heterospecific pregnancy with all its variants, normal as well as pathologic. For this purpose, two groups of cases were studied. The first group consisted of mothers and infants admitted without selection to a large obstetrical service and designated as the "obstetrical group." The second group, called the "pediatric group," was composed of all cases referred to us specifically for the diagnosis or possible exclusion of hemolytic disease due to anti-A or anti-B. The two groups were studied as far as possible in the same manner and by the same personnel. The maternal isoantibodies were investigated with a battery of techniques in the prepartal period, at term, and post partum. The antibody patterns of the newborn sera were compared with those of the mothers. The secretor status of the newborn infants with respect to A or B was determined, and the subgroup of A was established in the case of Group A infants whenever possible. The maternal history of pregnancies, transfusions, and immunization procedures was obtained. All infants were appraised on the basis of a general physical examination and were followed with determinations of hemoglobin and bilirubin levels. Hematologic studies were supplemented in selected cases with erythrocyte-survival studies in which the life span of transfused Group O and Group A or B cells was determined simultaneously.

It was hoped that this comprehensive approach might answer the question whether and under what conditions heterospecific pregnancy per se carries any disadvantages for the newborn infant or whether, indeed, it ordinarily produces recognizable effects on the offspring or on the maternal antibodies. It should then be possible to define what is to be considered abnormal in ABO incompatibility and to test the validity of various diagnostic criteria for ABO hemolytic disease. The further characterization of this condition might afford some insight into mechanisms and causes as yet obscure. The report was divided into several parts for purposes of clarity. The first part describes the methods used throughout the studies and deals with the case material and the maternal isoantibody patterns of the "obstetrical group."

CASE MATERIAL

A preliminary determination was made of the major blood groups of women attending the prenatal clinic of Herman Kiefer Hospital at the time of their first visit.* Group O mothers were selected on the basis of availability for further

* Dr. Charles Stevenson, Dr. Harold A. Ott and the obstetrical staff of Herman Kiefer Hospital, and Dr. G. M. Byington and the Department of Maternal, Child and School Health of the Department of Health assisted in this study.

studies and absence of any major medical or obstetrical complications. A complete typing for the Blood Groups ABO, M, N, and CDE was then performed, and a detailed obstetrical and medical history was obtained, with special emphasis on previous transfusions. A field worker then visited the women and obtained, whenever possible, blood for complete typings and saliva for a determination of the secretor status from the husband and any previous children. Serum specimens were obtained by venipuncture from the mothers at the time of the first contact and thereafter at monthly intervals, within 24 hours after delivery and again three weeks post partum. At the time of the first visit, a red blood cell count and a hemoglobin determination were likewise made. A record of the type of delivery and possible complications was kept.

The majority of the women (90%) were of the Negro race, and all belonged to the lower economic groups. There was a rather high incidence of illegitimacy and unknown paternity, and often the father of the current offspring was unknown or could not be located. The stage of pregnancy in which the patients first entered the prenatal clinic varied from case to case. Usually it was the end of the second or the beginning of the third trimester. The ages ranged from 14 to 40 years, with a preponderance of women in their late teens and early twenties. Sixteen of the mothers were Rh negative, and 139 were Rh positive. In the case of Rh-negative women, the presence of Rh antibodies was always excluded before the case was admitted to the study.

The cord bloods were collected for a determination of fetal blood group, Rh and M N type, subgroups of A in the case of Group A infants, hemoglobin content, red cell count, and serum bilirubin concentration. It was the obstetrical practice to allow the cord to pulsate for several minutes after delivery before ligating it. The newborn infant was given a pediatric examination within 12 to 24 hours after birth and again at the time of discharge, between the third and fifth day of life. At the age of 3 days, hemoglobin, red blood cell count, and bilirubin were again determined, this time from capillary blood obtained from a heel prick. At this point, a blood film was also made. In infants of Blood Group A or B, saliva was collected for the determination of the secretor status.

Three weeks later, a home visit was made, and the infant's blood was again tested for hemoglobin content and, occasionally, red cell count, and if the original typing had shown an A_2 reaction, the subgrouping procedure for A was repeated. If the result again indicated A_2, a final check was made at 6 months of age. At this time, the secretor status was also rechecked in all infants of Blood Group A or B who had previously behaved as nonsecretors.

A total of 155 women and infants were studied in this manner. In 92 cases the infant proved to be Group O. When it became apparent during the second year of the study that not enough heterospecific pregnancies would be found by this method of selection, additional cases were chosen at random from mass samplings of the cord bloods of newly delivered babies. Babies of Groups A or B whose mothers were found to belong to Group O were accepted until a total of 52 O-A and 60 O-B pregnancies was reached. In these cases, prepartal studies were of course not feasible, but all other procedures were carried out exactly as in the original group. In addition, 20 pregnancies of the types mother A-infant B or AB and mother B-infant A or AB were included in the study.

METHODS

1. *Typing Procedures.*—All serologic procedures were performed by the same person. The ABO grouping was done with dehydrated anti-A and anti-B rabbit sera (Lederle Laboratories Division, American Cyanamid Company) reconstituted in saline to give a titer of 1:64. For M and N typings, Lederle anti-M and -N rabbit sera were used, with a final titer of 1:64 against M and 1:16 against N. For Rh typing, serum of anti-D known specificity with a saline titer of 1:256 was available. Commercial anti-C and anti-E sera were obtained from Ortho Pharmaceutical Corporation and anti-c (hr) from Certified Blood Donor Service.

All typings except for c were done with saline suspensions prepared from whole blood. The erythrocytes were washed twice and resuspended in a 2% concentration in 0.9% NaCl. For AB and MN typings, one drop of antiserum was placed in each of four tests tubes and one drop of the 2% cell suspension to be tested was added to each tube. The tubes were briefly shaken in their racks and after standing at room temperature for 10 minutes were centrifuged at 500 rpm for 1 minute and read with the naked eye. Tubes showing no agglutination were checked microscopically before being recorded as negative. The subgroups of A were determined as follows.

Commercial anti-A_1 (absorbed B) serum obtained from Certified Blood Donor Service was placed in a deep-well slide and 1 drop of the test cell suspension added. The slide was then shaken mechanically at room temperature for 10 minutes. Cells showing no agglutination were recorded as belonging to subgroup A_2. Rh typing was performed by placing one drop of the appropriate serum anti-C, -D, or -E in each of three test tubes and adding the cell suspension. The tubes were incubated at 37 C. in a water bath for one hour, centrifuged for one minute, and read grossly and microscopically for agglutination. In selected cases, Du typing was carried out by incubating the cell suspension for one hour with anti-D serum and then performing the Coombs (antiglobulin) test on the thrice-washed cells. Testing for c was at first done in the manner described for C and D, with a serum of known anti-c specificity prepared in our laboratory. Later, only a commercial serum was available which had to be used against whole blood. A large drop of this serum was placed in a test tube. Blood was added with a wooden applicator to make an approximate 2% suspension, and the tube was placed in a water bath at 37 C. for three minutes, centrifuged for one minute, and gently shaken to dislodge cells sticking to the bottom. The reading was occasionally facilitated by the addition of 1 or 2 drops of saline.

2. *Secretor Tests.*—The determination of the secretor status from saliva was done by following essentially the method of Wiener.[1] Fresh saliva was used in all cases. Saliva specimens from infants were obtained by rolling a cotton swab inside the infant's mouth until it was thoroughly soaked and suspending it in 0.5 cc. of saline. The liquid was expressed from the swab and boiled for 10 minutes. In the case of adults and older children, larger volumes of saliva were collected in test tubes, boiled, and centrifuged. The supernatant liquid was used for the test in dilution of 1:10. Anti-A and -B typing serums of human origin were diluted 1:8 with saline. Tubes containing equal parts of the serum and saliva and control tubes containing only diluted serum and saline were allowed to stand at room temperature for 10 minutes. A 2% suspension of A or B cells was then added to each tube, and the mixtures were allowed to stand for one hour, centrifuged, and read for gross agglutination. In the control tubes, 4+ agglutination was observed. Saliva from secretors gave negative or very weak-positive (± or at most 1+) readings, nonsecretor saliva, readings of 3 to 4+. The reactions were always clear-cut.

3. *Anti-A and Anti-B Antibodies.*—A. Preparation of Test Cells: Throughout the study, standard test cells from the same constantly available donors of groups A_1, A_2, and B were used. Blood was obtained from these persons by weekly venipuncture. The specimens were divided into five samples before clotting. The tubes were kept in the refrigerator until used, and prior to actual testing the clots were not disturbed. Group O cells were obtained freshly as needed from a variety of Rh-positive and Rh-negative donors, since they served only to exclude atypical antibodies and there was no need for cells of constant characteristics. In addition to the

standard bloods, red corpuscles from the fathers of the patients and from the infants themselves were frequently used for comparison. In all instances, the cells remained in their native serum at 4 C. for not more than five days prior to testing.

B. The Preparation of the Sera: The maternal sera of the obstetrical group were stored in the Deepfreeze until all specimens, including the postpartum samples from a given woman, were collected. All the consecutive specimens were tested on the same day to insure a minimum of variation in the testing conditions. The sera from the cord bloods and those obtained from the mothers of the pediatric group, however, were tested, as a rule, immediately. All sera were inactivated at 56 C. for half an hour before titration.

C. Alpha and Beta Saline Agglutinin Titration: A series of serologic test tubes was labeled to contain dilutions of the serum to be tested, ranging from 1:8 to 1:16,000. Serial dilutions were made by transferring 1 cc. amounts from the first tube containing 1.75 cc. of 0.9% NaCl and 0.25 cc. of the serum to be tested. To labeled tubes containing 0.15 cc. of the serum dilutions, 0.1 cc. of the appropriate cell suspensions was added, and the tubes were briefly shaken manually and allowed to stand for one hour at room temperature, centrifuged at 500 rpm for one minute, and read macroscopically for agglutination. When cord sera were tested, the same procedure was followed, but the dilution series began with undiluted serum because of the lower alpha and beta titers expected in cord blood. The results of the readings were recorded as 4+ (single button of agglutinated cells), 3+ (large clumps), 2+ (medium and small clumps), or 1+ (small but grossly visible clumps). The saline agglutinin titers were not read microscopically. Each tube was examined by lightly flicking and read with the aid of a concave mirror.

Titration of anti-A and anti-B in gum acacia medium was carried out according to the method of Wiener and co-workers.[2] In parallel with the gum acacia technique, titrations were also carried out on many maternal sera of the obstetrical group by Wiener's plasma conglutination technique.[2] This procedure was abandoned in the course of the study because the results were less reproducible than those obtained by the acacia titration technique and, generally, the method was less sensitive.

D. Titration of Neutralized Sera (Witebsky Test): The alpha and beta saline agglutinins were neutralized with group-specific soluble substance (Sharp & Dohme, Inc.). During the early part of the study, an attempt was made in each case to neutralize the sera completely by adding the exact amount of group-specific substance necessary to abolish saline agglutination. In most sera this point was reached when the proportions of the mixture were between two and five parts of group-specific substance to one part of serum. Later, a 1:1 mixture often giving only partial neutralization was routinely used. The neutralized serum was titrated by the method of Witebsky.[3] A portion of the neutralized or partially neutralized serum was serially diluted with AB serum and titered against A_1, A_2, B, and O cells suspended in AB serum. A parallel titration of the serum in a saline system was carried out. On the tubes showing no macroscopic agglutinin in saline, the indirect Coombs test was carried out. The titers thus obtained closely parallel the results of the titration in AB serum.

E. Antiglobulin (Coombs's) Test: The direct and indirect Coombs test was carried out in the standard manner with serum (obtained from the Ortho Pharmaceutical Corporation). This rabbit serum had a titer of 1:64 when tested against cells sensitized with an undiluted human serum containing albumin (incomplete) Rh antibody. The rabbit serum when used undiluted produced agglutination of Rh-positive cells sensitized with dilutions up to 1:1,024 of a human anti-Rh serum which had an original albumin titer of 1:64.

The hemolysin test was done following the procedure of Mollison.[4] When stored sera were tested, fresh AB serum was used as a source of complement in which the A or B test cells were suspended before it was added to the suspected hemolytic serum.

F. Preparation of Eluates: Attempts were made to elute anti-A or anti-B from the fetal erythrocytes. The eluates were prepared from oxalated cord blood. The cells were washed three times in cold saline, suspended in an equal volume of 20% bovine albumin, and incubated at 56 C. for 10 minutes. The tube was centrifuged, and the supernatant fluid was tested against A_1, B, and O cells suspended in 20% albumin. The mixture was incubated for one hour at 37 C., centrifuged, and read for gross and microscopic agglutination.

OBSERVATIONS

I. Blood Groups and Secretor Status.—Of the 227 pregnancies in the obstetrical group, 223 resulted in the birth of living children. There were three stillbirths and one fetal death during labor as the result of an obstetrical complication. In none of the four cases of fetal death was it possible to determine the fetal blood group. The four mothers all belonged to Group O. The composition of the blood groups of the liveborn infants and of their mothers is shown in Table 1. Of the 52 infants of Blood Group A born to Group O mothers, 31 were typed as Subgroup A_1 at birth. Table 2 shows the results of subsequent typings on the infants who gave an A_2 reaction at birth. At 3 weeks of age, 3 of the 21 infants whose blood had given an A_2 reaction initially could be reclassified as belonging to subgroup A_1, and at 6

TABLE 1.—*Composition of the Blood Groups of the Liveborn Infants and Their Mothers*

Blood Group			Mother		Infant	
Mother	Infant	Total	Unip.	Multip.	Secretor	Nonsecretor
O	O	92	28	64	..	..
O	A	52	18	34	43	9
O	A_1	43	..	..	36	7
O	A_2	9	..	..	7	2
O	B	60	22	38	45	15
"Mixed" B	A	19	6	13	15	4
"Mixed" A	B					
"Mixed" A	AB					
"Mixed" B	AB					
Fetal deaths (fetal type unknown)		4	3	1		

TABLE 2.—*Results of Subgrouping of Fifty-Two Group A Infants at Various Age Levels*

	Birth	3 Wk.	6 Mo.*	Final Totals
A_1	31	3 ↑	7 ↑	41
A_2	21	→ 18	→ 9	9

* Two cases could not be located at 6 mo.

months, 7 more of the remaining infants with initial A_2 reactions proved to be A_1. Two infants could not be located at that time. Thus the total number of infants permanently classified as Subgroup A_2 was 9 out of 52, or approximately 20%, a figure which corresponds to the expected distribution of the subgroups of A. The two infants not available for checking at 6 months of age were added to the A_1 group in further tabulations because their siblings happened to be A_1, and the likelihood of their being A_1 was 4 : 1. The findings regarding the delayed appearance of A_1 characteristics in a substantial number of Group A newborn infants conformed to the observations of Witebsky and Engasser.[5]

Forty-three of the 52 Group A infants and 45 of the 60 Group B infants proved to be secretors (Table 1). No attempt was made to determine the secretor status of the 92 Group O infants. In 20 cases of Group A and Group B infants in which the original test had indicated nonsecretors, a check made six months later gave the same results as in the newborn period, confirming Wiener's [1] statement that the early determination of the secretor status is valid.

II. Homospecific Pregnancies.—A. Maternal Anti-A and Anti-B titers: Table 3 shows the anti-A and anti-B titers of the maternal sera of the group mother O-infant O. The titrations were carried out in parallel in saline and in gum acacia media. The ranges in both media correspond to those found in this laboratory in

TABLE 3.—*Maternal Anti-A and Anti-B Titers*

	Anti-A				Anti-B			
	Saline		Gum Acacia		Saline		Gum Acacia	
	Range	Median	Range	Median	Range	Median	Range	Median
1. Homospecific (O-O) Pregnancies								
Antepartum	8-512	128	16-2,048	256	8-256	64	16-512	128
Term	8-256	64	32-2,048	256	2-256	64	8-1,024	128
3 wk. p. p.	16-256	64	32-4,096	256	4-256	64	32-1,024	128
2. Heterospecific Pregnancy (O-A)								
Antepartum	8-256	64	32-1,024	256	8-128	32	16-512	128
Term	16-256	64	32-1,024	256	8-128	32	32-256	128
3 wk. p. p.	16-1,024	128	64-8,192	512	8-512	64	32-1,024	128
3. Heterospecific Pregnancy (O-B)								
Antepartum	16-512	128	32-1,024	256	16-512	64	32-1,024	256
Term	16-512	64	64-1,024	256	8-256	64	32-2,048	128
3 wk. p. p.	16-512	64	64-4,096	256	8-1,024	64	32-4,096	256

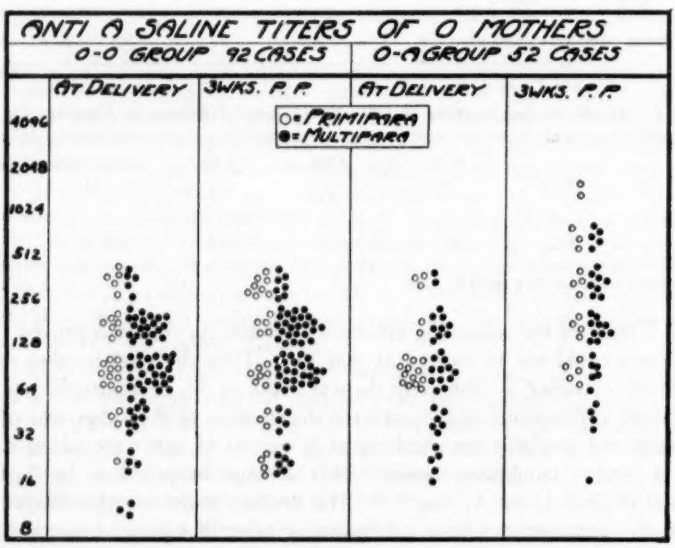

Chart 1

random sampling of nonpregnant adults. The titer in gum acacia was generally 1 to 2 units higher than that in saline. As illustrated for saline media in Charts 1 and 2, there was no difference in titers between primigravidae and multigravidae, regardless of whether the latter had previously borne children of Blood Groups A or B or had had only children of Group O. The titers remained stationary during

the progression of the individual pregnancies and also, as a rule, during the postpartum period. In two cases, there was a slight postpartum rise of both anti-A and anti-B saline and gum acacia titers following the birth of Group O children.

B. Titers of Partially Neutralized Sera (Witebsky Test): The presence of antibody capable of agglutinating A or B cells suspended in AB serum after partial neutralization of the test serum with group-specific soluble AB substance was

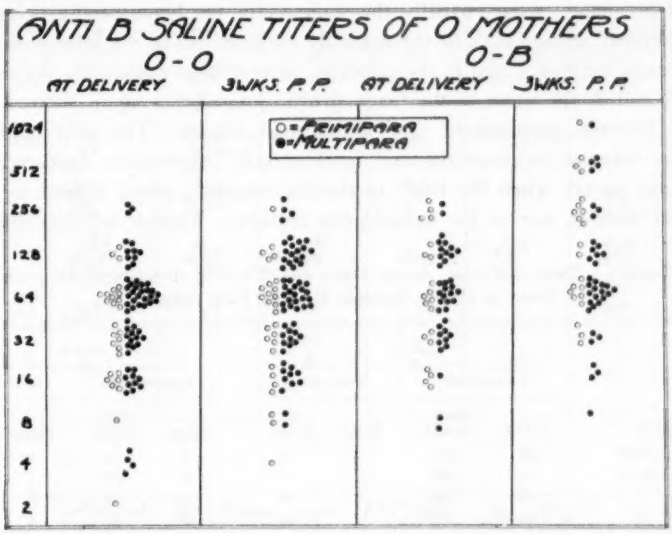

Chart 2

TABLE 4.—*Saline and Gum Acacia Titers and Witebsky Reaction of Maternal Serum in Case 1, Primigravida O, Infant O*

	Anti-A				Anti-B			
	Unmodified		Neutralized		Unmodified		Neutralized	
Serum	Saline	Gum Acacia	Saline	AB Serum	Saline	Gum Acacia	Saline	AB Serum
5 mo. b. t. d.*	512	4,096	8	256	256	512	0	0
3 mo. b. t. d.	256	1,024	8	256	64	128	0	0
Term	256	2,048	8	256	64	64	0	0
24 days p. p.	256	4,096	16	1,024	128	128	0	0
7 mo. p. p.	256	1,024	64	1,024	64	256	0	0

* Before term delivery.

looked for in every instance. A positive result was obtained with sera from two mothers of the homospecific (mother O-child O) group.

CASE 1 (No. 43).—Mrs. H. C., a 22-year-old Negro, Blood Group O, N, cDE, primigravida, never given transfusions, was first studied about five months before delivery. Table 4 shows that the anti-A saline and gum acacia titers were at the upper limit for the group but did not increase. The Witebsky test was positive from the beginning, with a titer of the neutralized serum 1:256 for anti-A which rose further to 1:1024 three weeks post partum, after the birth of a normal infant of Group O, N, cDe, and was unchanged seven months later.

CASE 33.—Mrs. T. G., an 18-year-old, Negro, secundagravida, never given transfusions, Group O, N, cDe, whose first child was Group O, N, cDE, had saline and gum acacia titers within the range of the group as a whole but a moderately strong Witebsky reaction which did not change significantly at term or post partum (Table 5).

III. Heterospecific Pregnancies.—A. Anti-A and Anti-B Titers: Table 3 (Parts 2 and 3) shows the titers of the maternal sera in the O-A and O-B heterospecific pregnancies. During the prepartal period and at term, the titers in both types of pregnancy were virtually the same as in the homospecific pregnancies. This statement applies both to the antibody antagonistic to the fetal blood group (homologous antibody) and to the opposite, heterologous agglutinin. As shown in Charts 1 and 2, the titers in the heterospecific pregnancies again showed no differences between primigravid and multigravid women. The only appreciable difference between homospecific and heterospecific pregnancies appeared in the postpartum period, when the titers in the heterospecific group tended to show a slight but distinct rise of the homologous antibody. Though in individual cases

TABLE 5.—*Saline and Gum Acacia Titers and Witebsky Reaction of Maternal Serum in Case 2, Secunda Gravida, Both Infants O*

	Anti-A				Anti-B			
	Unmodified		Neutralized		Unmodified		Neutralized	
Serum	Saline	Gum Acacia	Saline	AB Serum	Saline	Gum Acacia	Saline	AB Serum
2 mo. b. t. d.*	256	1,024	0	32	32	128	0	0
3 wk. b. t. d.	512	512	..	..	64	128	..	..
Term	256	512	0	16	64	256	0	0
3 wk. p. p.	256	512	2	64	128	256	0	0

* Before term delivery.

this rise rarely exceeded two units, the trend was clearly seen on inspection of both ranges and medians of the whole group (Charts 1 and 2, last vertical columns). The postpartum elevation was more marked for anti-A in the group with A infants than for anti-B in the mothers of B infants. The anti-B titers of the O-A group also showed a slight postpartum rise (Table 3, Part 2), but the anti-A titers of the mothers of B babies remained stationary (Table 3, Part 3). The gum acacia titers paralleled the saline titers in their general behavior.

The relationship between postpartum rise in titers and the type of pregnancy became more distinct when the subgroup and the secretor status of the infants were taken into consideration. As shown for the O-A group in Chart 3, the mothers of secretor infants of Subgroup A_1 showed significant postpartum elevations of the anti-A saline titers, exceeding two titration units in 6 of 43 cases. By contrast, the mothers of A_1 nonsecretor infants had stationary postpartum titers. The titers in the mothers of A_2 secretor infants showed only minimal changes. Again, the results of the saline titrations were paralleled by those of titration in gum acacia.

In the group of O mothers of B infants, the influence of the secretor status of the infant on the postpartum titer of the homologous antibody was as clearly evident as in the mothers of A_1 infants. Here, 12 of 45 secretor cases showed a postpartum rise, and none of the nonsecretor cases exhibited an increase in titer.

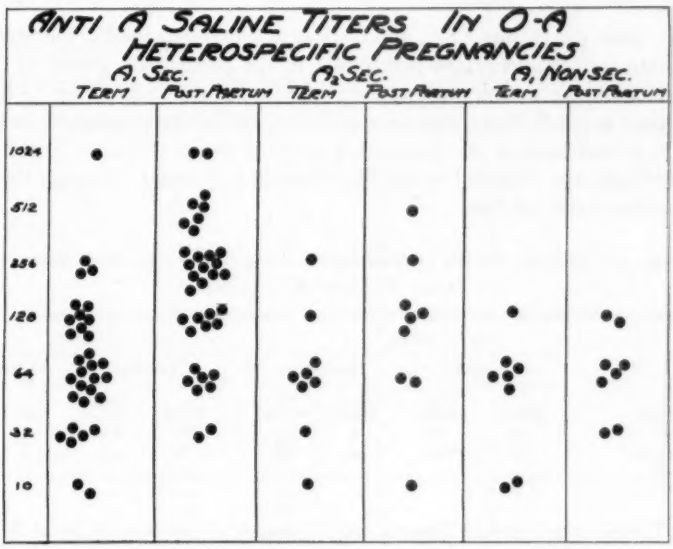

Chart 3

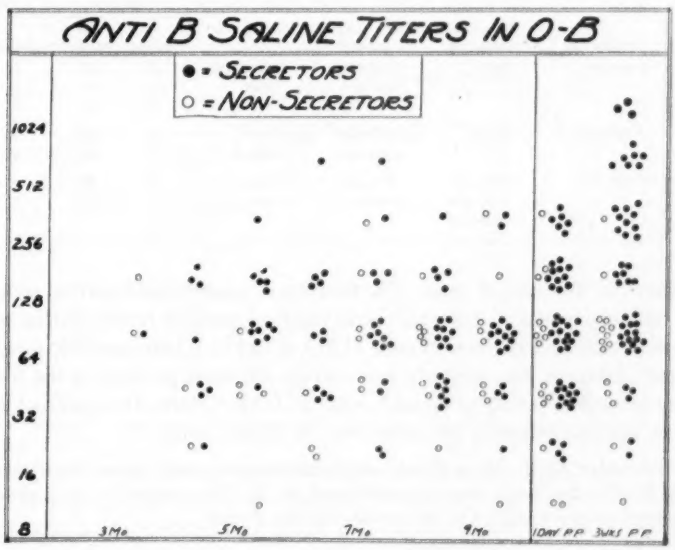

Chart 4

This relationship is illustrated in Chart 4, which also shows the stationary pattern of the homologous antibody in the prepartal period for both secretors and nonsecretors.

Thus, when the Groups O-A_1 and O-B were considered jointly, the titers of the homologous antibody increased perceptibly in the postpartum period in approximately 25% of the mothers of secretor infants. In one case of the O-A group, heterologous antibody titers rose concomitantly, and in three instances in the O-B group. In a single case of the nonsecretor group, a rise of two tubes of the heterologous antibody was observed in the O mother of a B infant, although the homologous antibody did not rise.

TABLE 6.—*Serologic Pattern of Maternal Serum in Case 3 (No. 359), Mother O, Infant A_2, Later A_1, Secretor*

	Anti-A				Anti-B			
	Unmodified		Neutralized		Unmodified		Neutralized	
Serum	Saline	Gum Acacia	Saline	AB Serum	Saline	Gum Acacia	Saline	AB Serum
Term	128	512	8	128	128	256	4	32
3 wk. p. p.	256	2,048	64	128	64	512	4	32

TABLE 7.—*Witebsky Reactions Showing Anti-A Antibody in Mothers of Group B Infants*

					Maternal			
					Anti-A		Anti-B	
Case	Mother	Previous Offspring	Infant		Saline	AB Serum	Saline	AB Serum
334	O M cDe	None	B M cDe	4 mo. a. p.	2	128	0	0
			Secretor	Term	2	64	0	0
				3 wk. p. p.	8	64	0	0
358	O MN cDE	None	B M cDE	Term	4	32	2	4
			Secretor	3 wk. p. p.	4	16	8	8
360	O MN cde	O M cDe	B M cDe	Term	2	32	8	32
		B N cDe	Secretor	3 wk. p. p.	0	8	2	4
		Secretor						

B. Titers of Neutralized Sera: The titration of neutralized maternal sera against A or B cells suspended in AB serum gave clear-cut positive results during gestation or at term in only four of the combined 112 O-A and O-B heterospecific pregnancies. In all four instances, the antibody was anti-A, although in three of the four cases the infant proved to belong to Blood Group B. Table 6 shows the maternal serologic pattern in the case in which the infant was of Blood Group A.

CASE 359.—Mrs. Q. R. was a 17-year-old Negro, unipara, never given transfusions, Blood Group O, M,CDe; her infant was originally typed A_2, M, CDe, retyped A_2 at 3 weeks of age, A_1 at 6 months, secretor, clinically and hematologically normal.

In an additional case (No. 290) of an O-A pregnancy, the anti-A of the maternal serum was consistently difficult to neutralize both before and after delivery, but titration in AB serum did not enhance the reaction (Table 6).

Table 7 shows Witebsky reactions against A with B infants in three cases. In five other cases, all in Group O mothers of Group B secretor infants, differences

of one to three tubes between saline and AB serum titers were observed ante partum, when the neutralized sera were tested against A and B cells. In none of these was the total height of the titers impressive, and none of these reactions were regarded as significant.

TABLE 8.—*Changes in Witebsky Reaction Against A and B in Postpartum Period, O-A Heterospecific Pregnancies*

		Anti-A		Anti-B	
Case		Saline	AB Serum	Saline	AB Serum
146	Term	0	0	0	0
	3 wk.	8	256	0	0
	2 mo.	8	256	0	0
	3 mo.	4	128	2	0
	6 mo.	16	16	4	4
201	Term	0	0	0	0
	3 wk.	8	64	0	0
	6 wk.	4	64	0	0
284	Term	2	2	0	0
	3 wk.	4	32	0	0
296	Term	2	4	0	0
	3 wk.	32	256	0	0
295	Term	8	8	0	0
	3 wk.	256	256	64	256
	6 wk.	128	128	32	64
	4 mo.	16	16	0	4

TABLE 9.—*Changes in Witebsky Reaction Against A and B in Postpartum Period, O-B Heterospecific Pregnancies*

		Serum Neutralized 1:1			
		Anti-A		Anti-B	
Case		Saline	AB Serum	Saline	AB Serum
109	Term	0	0	0	4
	3 wk.	0	32	2	32
354	Term	0	4	2	4
	3 wk.	8	16	512	1,024
	2 mo.	128	128	512	1,024
	6 mo.	4	32	128	178
363	Term	4	32	0	4
	3 wk.	8	16	0	16
116	Term	4	8	0	2
	3 wk.	16	64	16	64
335	Term	2	4	2	4
	3 wk.	8	8	256	512

In the postpartum period, the Witebsky test became frankly positive in four cases of the O-A group and in five cases of the O-B group (Tables 8 and 9). In one instance of an O-A pregnancy (Case 295, Table 8), the titer of the neutralized maternal serum rose sharply both in saline and in AB serum, though there was no appreciable difference between the two media. The table shows that in this case the anti-B Witebsky reaction also became positive, concomitantly with the anti-A reaction. In the group of O-B pregnancies, the appearance of anti-A Witebsky reaction paralleled that of the anti-B in four of the five cases. The rise in the heterol-

ogous antibody was always less marked than that of the antibody antagonistic to the infant's blood group, but was appreciable nevertheless. In the three cases in which a long-term follow-up was feasible, the titers of the Witebsky reaction fell significantly six to seven months after delivery.

There was no strict parallelism between the development of a positive Witebsky reaction and rising titers of the same sera in saline and gum acacia media. In two cases of the O-A group the anti-A titers rose appreciably when the anti-A Witebsky reaction became positive, in one case the rise was no greater than two units, and in two cases there was no rise in saline or gum acacia titer. Of the five cases of the OB group with postpartum Witebsky reactions, the titers rose in three and remained unchanged in two. Conversely, in the O-A pregnancies only two of the six sera with rising postpartum titers in saline and gum acacia developed a positive Witebsky reaction. In the O-B cases, a similar disparity was evident.

IV. "Mixed" Heterospecific Pregnancies.—The results in the mixed group consisting of 13 A mothers with 7 B and 6 AB infants and 6 B mothers with 4 A and 2 A_2 B babies were similar to those in the group of O mothers with hetero-

TABLE 10.—*Hemolysin Test with Sera of Random Donors Against Adult Test Cells*

	A_1	B	O		A_1	B	O
O	tr.	+	0	A	0	+	0
O	0	0	0	A	0	0	0
O	0	tr.	0	A	0	0	0
O	+++	0	0	A	0	+++	0
O	+++	0	0	A	0	0	0
O	+++	+	0	A	0	++	0
O	++++	+++	0	A	0	++	0
O	+++	0	0	A	0	+++	0
O	++	tr.	0	B	tr.	0	0
O	+	tr.	0	B	++++	0	0

specific offspring. In one case, that of an A_2 mother of a B secretor infant, the saline anti-B titer rose from 1:2 at term to 1:256 in the postpartum period and was still elevated six months later. In the Witebsky test the saline agglutinin became hard to neutralize, but there was no further enhancement when the titration was done in serum. In a second case, the serum of the B mother of an A_2 secretor infant showed a rise of saline anti-A agglutinin from 1:32 to 1:256, but the Witebsky reaction remained negative. None of the sera of the four mothers of nonsecretor infants changed before or after delivery.

V. Fetal Deaths.—The serologic findings in the four cases which terminated in fetal death gave no indication that the deaths were related to maternal isoimmunization. In each case, Rh sensitization was excluded by the maternal Rh type and by the negative antiglobulin test with a variety of Group O erythrocytes. The blood groups of the fathers were not obtainable. Two of the women were primigravidae, of the other two, one had two previous liveborn children, one of whom belonged to Blood Group B. The other mother had a liveborn child of unknown type and a previous stillbirth. The serologic patterns of none of the four women during pregnancy and at the time of delivery were remarkable. In one case, that of a unipara delivered of a 9 lb. (4,080 gm.) deadborn infant, the saline and gum acacia titers against both A and B were low at the time of delivery, but in the postpartum period the anti-A titer rose sharply and remained elevated for at least

seven months. Simultaneously, the Witebsky reaction became strongly positive. In the light of our other findings, it seemed reasonable to assume that the fetus was of Blood Group A and a secretor, but there was no evidence that a state of maternal isoimmunization existed prior to delivery. The attending obstetrician attributed fetal death to anoxia.

TABLE 11.—*Results of Hemolysin Test with Maternal Sera from the Obstetrical Group Tested Against Adult Test Cells*

Serum	Test Cells O-O Pregnancies				
	A_1	A_2	B	O	
Term	+++	+	0	0	
Term	+++	++	tr.	0	
Term	++	0	0	0	
Term	+	0	0	0	
Antep.	++	tr.	0	0	
Term	++	0	0	0	
Antep.	+	tr.	tr.	0	
Term	++	tr.	+	0	
P. p.	+	0	tr.	0	
Term	0	0	0	0	
P. p.	++	0	0	0	
Term	++	tr.	tr.	0	
P. p.	+++	tr.	0	0	
P. p.	+	0	0	0	
	O-A Pregnancies				
Antep.	tr.	0	0	0	
Term	0	0	0	0	
P. p.	+++	++	0	0	
Antep.	++	tr.	0	0	Infant secretors
Term	+	tr.	0	0	
P. p.	+++	++	0	0	
Term	0	0	0	0	
P. p.	+++	++	++	0	
Term	+	0	0	0	
P. p.	+	0	0	0	
Antep.	0	0	0	0	Infant nonsecretors
Term	0	0	0	0	
P. p.	0	0	0	0	
	O-B Pregnancies				
Antep.	tr.	0	++	0	Infant secretor
P. p.	..	..	+++	..	
Antep.	+	0	0	0	
Term	+	tr.	0	0	
P. p.	+	0	0	0	
Antep.	+	tr.	0	0	
Term	+	tr.	0	0	Infant nonsecretors
P. p.	+	0	tr.	0	
Antep.	tr.	0	0	0	
Term	tr.	0	0	0	
P. p.	tr.	0	0	0	

VI. Hemolysins.—Mollison [4] recently demonstrated hemolysis of A or B cells by sera of mothers thought to be sensitized against A or B antigens with resultant hemolytic disease in the offspring. The evaluation of this technique in the obstetrical group was limited to a small number of cases, since the study was already well under way when the method was introduced.

In a preliminary survey, sera from 20 random adult nonpregnant donors were tested against adult A_1 and B cells. As Table 10 indicates, a large percentage of such sera contained hemolysins against A_1 or B. The sera of 14 mothers of the obstetrical group with both O-O and O-A or O-B pregnancies (Table 11) like-

TABLE 12.—*Results of Hemolysin Test with Adult and Cord Test Cells*

Obstetrical Group O-A Infants		Adult Cells		Cord Cells		Adult Cells
A1 Secretor		A1	A2	A1	A2	O
	Antep.	++	Tr.	+	0	0
	Term	++	Tr.	+	0	0
	P. p.	+++	++	++	+	0
	Antep.	Tr.	0	0	0	0
	Term	Tr.	0	0	0	0
	P. p.	++	....	+	..	0
	Antep.	++	+	+	Tr.	0
	Term	+++	++	++	Tr.	0
	P. p.	+++	++	++	Tr.	0
	Antep.	Tr.	0	Tr.	0	0
	Term	Tr.	0	Tr.	0	0
	P. p.	+++	++	++	+	0
	Antep.	+	0	Tr.	0	0
	Term	+	0	0	0	0
	P. p.	+++	++	++	Tr.	0
	Antep.	+++	+	++	0	0
	Term	+++	+	++	0	0
	P. p.	+++	+	++	0	0
	Antep.	Tr.	0	0	0	0
	Term	Tr.	0	0	0	0
	P. p.	+++	+	....	Tr.	0
	Antep.	+	0	Tr.	0	0
	Term	+	0	Tr.	0	0
	P. p.	+++	Tr.	+	Tr.	0
	Antep.	+	—	Tr.	0	0
	Term	Tr.	0	0	0	0
	P. p.	+++	++	++	Tr.	0
	Antep.	+++	++	++	Tr.	0
	Term	++	+	++	Tr.	0
	P. p.	+++	+++	+++	Tr.	0
	Antep.	++	0	+	0	0
	Term	0	0	0	0	0
	P. p.	+++	+	++	Tr.	0
A2 Secretor	Antep.	+	0	Tr.	0	0
	Term	Tr.	0	0	0	0
	P. p.	+	0	Tr.	0	0
	Antep.	++	0	Tr.	0	0
	Term	+	0	Tr.	0	0
	P. p.	++	0	Tr.	0	0
	Antep.	Tr.	0	Tr.	0	0
	Term	0	0	0	0	0
	P. p.	0	0	0	0	0
	Antep.	Tr.	0	0	0	0
	Term	++	Tr.	+	0	0
	P. p.	++	Tr.	+	—	0
	P. p.	0	0	0	0	0
	Term	Tr.	0	0	0	0
	P. p. (previous "O" infant)	0	0	0	0	0

wise showed hemolysins. In several instances there were distinct increases in the hemolytic activity of the maternal serum during the postpartum period. This phenomenon was observed in mothers of O babies, as well as in the O-A and O-B groups. In the latter cases, however, it was limited to the mothers of secretor infants.

Because of the frequency of hemolysins affecting adult A_1 cells, Mollison † has suggested the use of fetal cells obtained from cord blood in order to make the test significant with respect to fetal disease due to maternal isoimmunization against A or B. The sera of 16 Group O mothers of A babies were tested simultaneously against adult A_1 and A_2 and cord A_1 and A_2 blood. Table 12 shows a graded reaction of the different cells, with the individual sera adult A_1 showing the most marked hemolysis, adult A_2 and cord A_1 giving similar but consistently weaker reactions. Cord A_2 blood was not hemolyzed even by sera producing +++ hemolysis against adult A_1. In the prepartal period, 5 of the 16 sera produced + + to+ + + hemolysis of adult erythrocytes, but only 2 of these hemolyzed A_1 cord cells. At term the findings were unchanged, but 13 of the sera obtained three weeks post partum hemolyzed adult A_1 cells and eight of these also cord A_1 cells. In each case the infant was a secretor of subgroup A_1.

The results of this limited experience with the hemolysin test were generally in keeping with those obtained by the other methods designed to demonstrate so-called immune anti-A or anti-B. The fact that maternal sera frequently became hemolytic in the postpartum period if the infant proved to be a secretor was comparable to the rise of saline or gum acacia titers and to the appearance of the Witebsky phenomenon in the same period in mothers of secretor infants. It is noteworthy that the three serologic reactions did not always parallel each other. Each occurred in the absence of the other two. The number tested was insufficient to compare multiparae and uniparae with respect to hemolysis.

COMMENT

As expected, homospecific pregnancy had no measurable effect on the maternal anti-A and anti-B antibodies either during gestation or after delivery. The titers of the saline agglutinins showed the usual variation from person to person over a fairly wide range, but for each person the level was virtually constant throughout the period of observation. Since multigravidae had titers of the same range and distribution as primigravidae even if their previous children belonged to Blood Group A or B, there was no evidence in this material for a prolonged effect of preceding heterospecific pregnancy on the saline agglutinins measured during a later homospecific pregnancy.

The two cases of homospecific pregnancy in which the maternal sera showed properties generally regarded as characteristic of immune anti-A, such as a positive Witebsky reaction, were of particular interest.[3] Neither of the two Group O mothers had previously born A or B children, one being a unipara, the other having had one child belonging to Group O. The nature of the possible antigenic stimulus responsible for the sustained presence of immune anti-A in both cases was obscure. The serologic findings placed these subjects in the category of so-called dangerous universal donors described by Witebsky, Ervin and Young,[6] and others. In the

† Mollison, P. L.: Personal communication to the authors.

cases reported in detail by Ervin and Young, the donors were Group O men and one Group O woman whose husband was likewise Group O. The authors were likewise unable to account for the presence of immune anti-A. Obviously, the "spontaneous" occurrence of such immune bodies in male donors and in women who have not gone through heterospecific pregnancies has a bearing on the interpretation of immune anti-A or anti-B found during or after pregnancies which happen to be heterospecific.

In the group of heterospecific pregnancies, the maternal antibody patterns during the period of gestation showed no more response than did those of the homospecific group. The range and distribution of the saline titers were the same, and no significant increases occurred up to the time of delivery. In this respect our findings are in agreement with the observations of most previous investigators.‡ Only Smith [8] reported increases in saline titers in the mothers of secretor infants of Blood Groups A and B toward the end of gestation. Actually, the increases observed by him were so small as to be of doubtful significance.

Nearly all of the earlier reports on isoantibodies in heterospecific pregnancy dealt with the behavior of saline agglutinins.[9] Lately it has become clear that immune anti-A or anti-B may be present in sera with saline agglutinins of only low or average titer. It was for this reason that the present study included observations designed to test for immune anti-A or anti-B in every serum, in parallel with the titration of the saline agglutinins. Anti-A with immune characteristics was found in 4 of the 112 Group O mothers of heterospecific children. In at least three of these cases its presence was unrelated to fetal blood-group antigens, however, since the three infants proved to belong to Blood Group B. Moreover, two of the three mothers were uniparae, while the third had previously given birth only to one Group O and one Group B child. The situation was therefore comparable to that in the two mothers of Group O infants referred to above and to that in male "dangerous universal donors." In view of the finding of immune anti-A in five mothers of Group O and Group B children, the presence of such antibody in a single instance of an O-A heterospecific pregnancy cannot be regarded as proof that in this case the Group A fetus had caused the maternal immunity. The mother was a unipara without previous history of transfusions. Unfortunately, no prepartal studies were made in this particular instance. In none of the cases of heterospecific pregnancy in which the antibodies were followed serially was anti-A or anti-B immune antibody observed to develop *de novo* in the course of a pregnancy.

The stationary patterns of the maternal isoantibodies up to the time of delivery indicate that the heterospecific fetus during gestation does not ordinarily act as an effective antigenic stimulus. By contrast, the frequent changes occurring in the postpartum period must be interpreted as evidence that events connected with the termination of heterospecific pregnancy may produce a more or less specific antigenic effect. These responses were least evident in the behavior of the saline agglutinin titers. The increases were generally small, of the order of one to two units, and their significance in the individual case would be open to question. The trend toward an elevation of the saline titer was clear-cut, however, when the group as a whole was considered. We did not observe the tremendous elevations of the postpartum titers up to 256,000 reported by Boorman and her associates.[10]

‡ Witebsky, E.: Personal communication to the authors, and Reference 7.

The appearance of a positive Witebsky reaction in a number of cases in which this test had been negative ante partum or at term furnished even more definite evidence of an immune response, since it was usually the antibody antagonistic to the infant's blood group which showed the main reaction. The frequent occurrence of a lesser concomitant response of the heterologous antibody shows, however, that the effects of the stimulus are not altogether specific. Rather, as with interrelated bacterial and viral antigens, a sort of cross reaction seems to take place.

In some instances the titration of the neutralized serum in the Witebsky reaction revealed an increasing resistance of the saline agglutinins to the neutralizing effect of AB soluble substances, rather than the more typical discrepancy between a low saline titer and a much higher titer in AB serum. Because this kind of response occurred in the same groups and at the same time in relation to delivery as did the typical positive Witebsky reaction, it may be assumed that it has the same significance.

In general there was good agreement between the various tests designed to show antibody responses. The results were not invariably parallel, however, and any one method might fail in a case in which the others showed a reaction. The titration of "conglutinins" in gum acacia, apart from being technically somewhat more difficult, generally seemed somewhat less sensitive than other methods. On the other hand, the hemolysin test in our hands proved to be rather too sensitive. Obviously, hemolysis of adult A_1 cells by Group O sera is too common to be of diagnostic significance. The experience of Mollison with the use of cord blood as a less sensitive substrate for this test was substantiated by our limited observations with the hemolysin technique. The chief obstacle to the application of this test would seem to lie in the difficulty of classifying newborn Group A cells according to the subgroup; since in our material the hemolysins reacted more strongly with A_1 cells, cord blood reacting like A_2 might give false-negative results.

The occurrence of postpartum responses of the maternal anti-A and anti-B antibodies was limited to the mothers whose infants proved to be secretors with respect to the properties A or B. The significance of the secretor status of the offspring for the maternal isoantibodies was first noted by Smith, in a study of saline agglutinins, and was shortly confirmed by Jakobowicz and Bryce.[9] Our observations show that the relationship between maternal antibody response and secretor status of the infant holds not only for saline agglutinins but for all types of antibody reactions investigated. No postpartum rises were observed in any of the mothers of nonsecretor infants. It should be noted, on the other hand, that in our material and in the experience of the Australian authors the birth of a heterospecific secretor infant was followed by a measurable antibody response only in the minority of cases. Smith [8] believed that such a response occurred regularly. Our findings suggest, however, that the effective antigenic stimulation of the mother is a special event rather than the rule, even in the presence of a secretor fetus. Smith further assumed that the antigenic stimulus was provided by the passage of soluble group-specific substances, elaborated only by secretor fetuses, across the placenta during gestation. Our results indicate that the stimulation takes place not during gestation but during labor. The postpartum responses are compatible with the hypothesis that the fetal antigens gain entrance into the maternal circulation by absorption from the retroplacental space during the third stage of labor.

The fact that the antibody responses are limited to mothers of secretor infants indicates that absorption of soluble group-specific substance is the stimulus, as postulated by Smith. The failure of nonsecretor infants to provide such a stimulus must mean either that whole erythrocytes do not enter the maternal circulation or that in spite of their content in A or B substance they are not effective antigens. The first of these possibilities conflicts with the current theory of Rh isoimmunization which assumes that whole erythrocytes as the sole carriers of antigen provide the stimulus and therefore do enter the maternal circulation. The failure of whole erythrocytes to act as effective stimuli for anti-A or anti-B would suggest, therefore, that erythrocyte A or B substances are poor antigens compared with soluble A or B substances in plasma or serum. This reasoning is in keeping with present evidence regarding the comparative antigenic potency of red corpuscles and serum.[11]

The observations on O-A pregnancies establish a difference in the maternal response depending on the subgroup of the infant. In all cases in which the Witebsky reaction became positive post partum or in which rises of more than two units developed in the saline agglutinin titers, the infants were Subgroup A_1 secretors. The secretor status did not affect this observation, since none of the cases in which the infants were secretors of Subgroup A_2 showed similar responses. The significance of the subgroup of the A infants for the maternal response appears to have escaped the attention of earlier investigators, probably because of the difficulty in establishing reliably at birth the subgroup of those infants whose initial reactions are those of A_2. As Witebsky and Engasser [5] have shown, the erythrocytes of newborn Group A infants frequently react like A_2 cells, though later the same infants prove to be A_1. Only newborn bloods giving A_1 reactions can therefore be permanently classified at that time. The apparent limitation of postpartum antibody responses to the mothers of A_1 infants is particularly interesting in view of the apparent A_1 specificity of the anti-A immune antibody.§

The question needs to be considered whether the antibody responses against A or B which may occur in the wake of heterospecific pregnancy are lasting and if so whether they are significant with respect to the outcome of subsequent heterospecific pregnancies, as are the antibody responses to Rh. The evidence on this point is inconclusive. Polayes and McNally [12] found a somewhat higher range of saline anti-A and anti-B titers in multiparous than in nulliparous women. The differences were, however, only of the order of one to two titration units, and the titers appeared insignificant in comparison with those obtained by the same authors in cases of ABO hemolytic disease. Jonsson [13] studied anti-A and anti-B hemolysins in the sera of Group O women and compared mothers of A or B children with mothers of O children. He found an appreciably higher incidence of hemolytic sera in the heterospecific group. These findings suggest a persistence of the effect of heterospecific pregnancy in the maternal antibody pattern. This effect, however, must ordinarily be minor and without clinical significance, since most heterospecific infants born to multiparous women show no effects of maternal isoimmunization against A or B. Our own observations disclosed no differences in the range and distribution of saline titers and gum acacia titers or in the incidence of "immune"

§ References 3 and 5.

anti-A or anti-B between nulliparous women and mothers of only previous O children on the one hand and multiparous women, including mothers of known A and B children, on the other.

Boorman and her associates have commented on the similarity of the agglutinin response following heterospecific pregnancy to that following the injection of incompatible blood. In both cases, a peak of the titer is reached in one to three weeks, after which time there is a progressive decline. Unfortunately, the reported observations on persons known to have received incompatible blood usually extend only over a relatively short period of acute titer changes. We were unable to find information about the titers in such cases after long intervals, such as one or more years, which would be pertinent. Likewise, the persistence of immune type anti-A or -B over such periods following known stimuli is not adequately documented. In the four cases of the present study in which the antibodies developing in response to heterospecific pregnancy could be followed for as long as six to seven months, all reactions tested showed a decline toward the levels found at term, though as yet those levels had not been reached. Thus far there seems to be no evidence either in the literature or in our data that the frequent postpartum responses of heterospecific pregnancy regularly or usually produce a cumulative effect on the serum antibodies or on the fetus in subsequent heterospecific pregnancies in a manner comparable to the progression of events in Rh immunization.

From the diagnostic point of view, the difficulty in the interpretation of titers or immune reactions against A or B obtained in the postpartum period is obvious. Findings at that time do not constitute evidence that significant antibodies were present at birth and therefore that symptoms observed in the infant are necessarily due to maternal isoimmunization against A or B. The presence of exceptional titers or immune antibodies at term or prenatally would be more significant but of course cannot be evaluated until the blood group of the infant is known. The interpretation of such serologic findings in relation to ABO hemolytic disease will be discussed in a subsequent paper.

SUMMARY

The patterns of isoantibodies against A and B were investigated with several techniques in 224 pregnancies, chiefly in Group O mothers. In homospecific pregnancy Type O-O the patterns were stationary before and after delivery. In heterospecific pregnancy the same range of titers was found, and the patterns likewise remained stationary during gestation and term. In the postpartum period a minority of cases of heterospecific pregnancy exhibited a specific immune response to the fetal blood-group antigen. These responses occurred only in the mothers of secretor infants and in the case of Group A infants only if the infant belonged to subgroup A_1. The responses consisted in slight to moderate elevations of the saline titers, parallel changes in the gum acacia ("conglutinin") titers, appearance of antibody demonstrable in serum media or by the indirect Coombs test after "neutralization," and appearance of hemolysins. A nonspecific response of the opposite antibody frequently accompanied the response shown by the antibody antagonistic to the fetal blood group.

In a few cases in which long-range postpartum follow-up was possible, the response was subsiding but had not yet completely disappeared as late as seven months after delivery. The antibody patterns of multiparous Group O women with

previous A or B children, however, showed no evidence of a persistent effect of earlier heterospecific pregnancies. Thus, heterospecific pregnancy may be followed by an immune response if the infant is a secretor, but there is no evidence that such responses when caused by pregnancy ordinarily persist or affect unfavorably the outcome of future pregnancies.

The observed facts suggest that the antigenic stimulus occurs during labor and is supplied by soluble specific substances rather than by whole erythrocytes.

The finding of high titers or immune types of isoantibodies in the postpartum period is of limited diagnostic value because of the occurrence of immune responses after normal heterospecific pregnancy. In both homospecific and heterospecific pregnancy, the maternal serum occasionally exhibits immune properties against A. In five of the six pertinent cases, however, the possible effect of fetal antigen from the present or earlier pregnancies would be excluded, and in all cases the nature of the antigenic stimulus was obscure. These women were regarded as "dangerous universal donors."

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ABO HETEROSPECIFIC PREGNANCY AND HEMOLYTIC DISEASE

A Study of Normal and Pathologic Variants

II. Patterns of A and B Isoantibodies in the Cord Blood of Normal Infants

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IN THE PRECEDING paper,[1] the anti-A and B isoantibody patterns of unselected women in homospecific and heterospecific pregnancies were described. The present paper deals with the infants born to those mothers and is concerned with the isoantibodies of the cord bloods and their relationship to the maternal isoantibodies. The methods used were the same as those described in the first paper.

OBSERVATIONS

Homospecific Pregnancies.—Cord bloods for isoantibody studies were available from 69 of the 92 Group O infants of O mothers. In 23 cases the cord serum could not be obtained either because the child had been delivered at home or in another hospital or because of accidental losses in collecting the samples. The results of the anti-A and anti-B titrations of the 69 cord sera are given in Table 1, together with the corresponding maternal titers drawn within 24 hours after delivery. It will be seen that both α and β antibody was demonstrable in the vast majority of the cord sera. In the saline media, anti-A was demonstrated in 67 and anti-B in 61 of the 69 specimens. With the acacia titration, anti-A was demonstrated in all cord sera and anti-B in all but one case. Thus, with the latter technique the complete antibody pattern of the maternal serum was virtually always qualitatively reflected in the cord blood.

Quantitatively, the cord-blood titers against A showed the same general relationship to those against B as did the maternal titers. The range for saline titers against both A and B was 0 to 128, but the β titers were generally lower. In 26 of the 61 cord sera with anti-B saline activity the β agglutinin could be demonstrated only in the undiluted serum, whereas α agglutinins of such low titer were found only six times.

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TABLE 1.—*Anti-A and Anti-B Titers of Maternal and Cord Sera of Group-O Mothers and Group-O Infants*

	Anti-A						Anti-B					
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
	Saline, Maternal		Gum Acacia, Maternal		Difference in Saline & Gum Acacia Titers, No. of Tubes		Saline, Maternal		Gum Acacia, Maternal		Difference in Saline & Gum Acacia Titers, No. of Tubes	
Case	Cord	Ratio	Cord	Ratio	Maternal	Cord	Cord	Ratio	Cord	Ratio	Maternal	Cord
Ad	64	16	128	1	1	5	32	32	64	16	1	2
	4		128				1		4			
And	128	2	512	4	2	1	64	4	256	4	2	2
	64		128				16		64			
Ant	64	8	256	4	2	3	16	8	64	2	2	2
	8		64				2		32			
Ar M.	64	32	128	4	1	4	32	32	128	4	2	5
	2		32				1		32			
Ar R.	32	8	128	2	2	4	8	8	64	8	3	3
	4		64				1		8			
Be	64	32	128	4	1	4	8	— 8	32	32	2	1
	2		32				0		1			
Bl	64	32	128	16	1	2	64	—64	64	16	0	2
	2		8				0		4			
Bra	64	16	256	16	2	2	16	—16	32	8	1	2
	4		16				0		4			
Broo	128	64	512	64	2	2	64	64	256	128	2	1
	2		8				1		2			
Brow	64	32	256	4	2	5	32	32	128	8	2	4
	2		64				1		16			
Ca	128	16	256	2	1	4	256	16	256	2	0	3
	8		128				16		128			
Ch C.	64	8	256	2	2	4	64	32	128	4	1	4
	8		128				2		32			
Ch L.	64	16	256	16	2	2	64	32	128	32	1	1
	4		16				2		4			

Chr	64	64	256	16	2	4	16	16	128	64	3	1	
	1		16				1		2				
Cla	128	16	512	8	2	3	128	64	512	64	2	2	
	8		64				2		8				
Cle	16	16	32	2	1	4	64	32	128	4	1	4	
	1		16				2		32				
Co	256	2	4,096	8	4	2	64	64	128	16	1	3	
	128		512				1		8				
Cr	8	4	128	2	4	5	8	8	32	2	2	4	
	2		64				1		16				
Da	128	64	512	8	2	5	256	16	1,024	4	2	4	
	2		64				16		256				
Doc	64	32	256	8	2	4	64	64	256	16	2	4	
	2		32				1		16				
Dom 1	32	32	64	4	1	4	32	32	64	32	1	1	Twins
	1		16				1		2				
Dom 2	32	16	64	4	1	3	32	−32	64	64	1	1	
	2		16				0		1				
Dun	128	8	512	4	2	3	64	16	64	4	0	2	
	16		128				4		16				
Dup	64	64	128	64	1	1	64	64	64	8	0	3	
	1		2				1		8				
Es	16	4	128	4	3	3	32	4	128	8	2	1	
	4		32				8		16				
Fi	256	32	512	8	1	4	128	64	512	32	2	3	
	4		64				2		16				
Fit	128	64	256	16	1	3	64	−64	128	32	1	3	
	2		16				0		4				
Grah	128	8	512	2	2	4	32	16	128	8	2	3	
	16		256				2		16				
Gran	64	32	512	64	3	2	32	−32	128	64	2	2	
	2		8				0		2				

TABLE 1.—*Anti-A and Anti-B Titers of Maternal and Cord Sera of Group-O Mothers and Group-O Infants* — Continued

	Anti-A						Anti-B					
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
	Saline, Maternal / Cord	Ratio	Gum Acacia, Maternal / Cord	Ratio	Difference in Saline & Gum Acacia Titers, No. of Tubes: Maternal	Cord	Saline, Maternal / Cord	Ratio	Gum Acacia, Maternal / Cord	Ratio	Difference in Saline & Gum Acacia Titers, No. of Tubes: Maternal	Cord
Gre	256 / 16	16	512 / 256	2	1	4	64 / 2	32	256 / 64	4	2	5
Ha	64 / 4	16	128 / 32	4	1	3	16 / 1	16	64 / 16	4	2	4
He	8 / 4	2	32 / 64	0.5	2	4	2 / 0	— 2	8 / 4	2	2	3
Hood	256 / 32	8	256 / 64	4	0	1	32 / 1	32	64 / 8	8	1	3
Hook	32 / 8	4	128 / 64	2	2	3	64 / 4	16	128 / 16	8	1	2
Hu	128 / 8	16	512 / 128	4	2	4	64 / 2	32	128 / 16	8	1	3
Ja	64 / 4	16	512 / 16	32	3	2	64 / 2	32	128 / 16	8	1	3
Je	128 / 16	8	256 / 32	8	1	1	128 / 4	32	256 / 16	16	1	2
Jo D.	64 / 2	32	64 / 16	4	0	3	16 / 1	16	64 / 16	4	2	4
Jo M.	64 / 2	32	512 / 16	32	3	3	64 / 2	32	128 / 4	32	1	1
Jo R.	128 / 32	4	512 / 256	2	2	3	32 / 2	16	64 / 32	2	1	4
Jon	64 / 8	8	512 / 32	16	3	2	64 / 1	64	128 / 4	32	1	2
Ke	32 / 0	—32	128 / 16	8	2	5	32 / 0	—32	64 / 4	16	1	3

La	32/1	32	128/4	32	2	2	8/1	8	32/8	4	2	3
Le	256/8	32	512/64	8	1	3	64/1	64	128/4	32	1	2
Ll	128/2	64	128/16	8	0	3	32/4	8	128/8	16	2	1
Lo	64/2	32	512/32	16	3	4	128/2	64	512/32	16	2	4
Mc	64/2	32	256/16	16	2	3	128/4	32	512/8	64	2	1
Mon	256/16	16	512/512	1	1	5	32/2	16	128/32	4	2	4
Mor	32/16	2	512/256	2	4	4	8/2	4	32/32	1	2	4
Na	128/8	16	1,024/64	16	3	3	64/1	64	256/4	64	2	2
Ne	16/0	—16	64/16	4	2	5	64/2	32	256/32	8	2	4
Nu	64/2	32	128/32	4	1	4	16/2	8	64/8	8	2	2
Ow	128/2	64	256/16	2	2	3	256/4	64	512/16	32	1	2
Perk	64/16	4	256/128	2	2	3	16/2	8	32/8	4	1	2
Perr	128/2	64	256/16	16	1	3	128/16	8	512/128	4	2	3
Re R.	64/4	16	256/64	4	2	4	128/2	64	256/16	16	1	3
Re W.	16/16	1	128/64	2	3	2	64/1	64	256/4	64	2	2

TABLE 1.—*Anti-A and Anti-B Titers of Maternal and Cord Sera of Group-O Mothers and Group-O Infants*—Continued

	Anti-A						Anti-B					
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
	Saline, Maternal		Gum Acacia, Maternal		Difference in Saline & Gum Acacia Titers, No. of Tubes		Saline, Maternal		Gum Acacia, Maternal		Difference in Saline & Gum Acacia Titers, No. of Tubes	
Case	Cord	Ratio	Cord	Ratio	Maternal	Cord	Cord	Ratio	Cord	Ratio	Maternal	Cord
Se	128	16	256	2	1	4	64	—64	128	—128	1	..
	8		128				0		0			
Sl	64	16	256	4	2	4	32	16	64	4	1	3
	4		64				2		16			
Sm	64	32	256	8	2	4	16	2	64	4	2	1
	2		32				8		16			
Sn	32	8	128	8	2	2	16	16	64	16	2	2
	4		16				1		4			
Te	32	32	64	8	1	3	32	32	64	32	1	1
	1		8				1		2			
Tu	64	2	256	1	2	3	32	32	128	32	2	3
	32		256				1		4			
Welc	128	8	512	2	2	4	16	8	64	4	2	3
	16		256				2		16			
Well	128	2	1,024	2	3	3	64	32	256	16	2	3
	64		512				2		16			
Wl D.	256	32	1,024	8	2	4	128	64	256	8	1	4
	8		128				2		32			
Wl J.	64	8	256	2	2	4	64	16	256	4	2	4
	8		128				4		64			
Wil	32	32	64	4	1	4	32	32	256	32	3	3
	1		16				1		8			
Yo	128	32	512	16	2	3	64	64	128	16	1	3
	4		32				1		8			

While the relationship between the α and β agglutinins in the cord bloods thus reflected in a general way the pattern of the maternal agglutinins, the ratios of the maternal to the cord-blood titers varied widely from case to case. The maternal-fetal titer ratios ranged from 1 : 1 to 64 : 1, irrespective of the absolute values of the titers (Table 1, Columns II and VIII). When the fetal titer was less than 2, the maternal titer was also low or moderate, not exceeding 64, but the reverse was not consistently true, i. e., low maternal titers were not necessarily associated with minimal cord-blood titers. Thus, a maternal titer of 64 might be found with a cord titer of 1 in one case and 32 in another. In one instance the maternal anti-A titer of 1 : 16 was identical with the titer found in the cord blood. Clearly the height of the maternal titer alone did not determine that of the fetal titer but merely governed its upper limit. Other factors, presumably residing in the placenta and varying from case to case, seemed to be influencing the maternal-fetal ratios. The ratios were generally similar, if not identical, for α and β antibody in a given case.

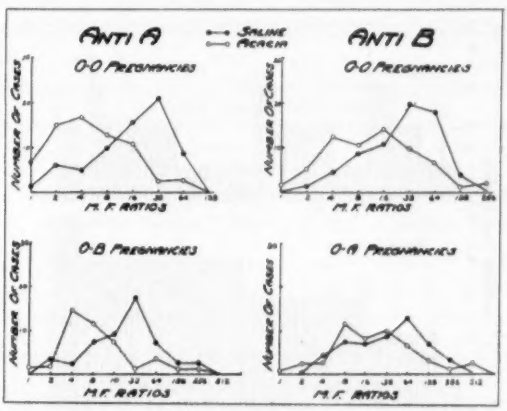

Chart 1.—Ratios of maternal to fetal titers in saline media (solid circles) and in gum acacia media (open circles) in various types of pregnancy. It is shown that in each type of pregnancy the ratios of the saline titers between mother and child tend to be high, indicating poor but variable passage across the placenta, as compared with the ratios of the gum acacia titers, which tend to be low, indicating greater placental permeability for this type of antibody.

The gum acacia ("conglutinin") titers of the cord sera ranged from 2 to 512 for anti-A and 0 to 256 for anti-B (Table 1, Columns III and IX). Again, the anti-A titer in the individual cases was usually higher than the anti-B titer. The ratios of the maternal to the fetal titers determined in gum acacia medium were also quite variable (Table 1, Columns IV and X), but in general were lower than the ratios of the saline titers of mother and fetus. Though in some cases the maternal-fetal ratios were identical in the two media, nevertheless, as shown in Chart 1, most of the saline ratios were high and most of the gum acacia ratios low. The trend was sufficiently clear cut to suggest that the antibody measured by titration in gum acacia could pass the placenta more readily than the saline agglutinin. Moreover, the trend was evident for anti-B as well as anti-A, although it was less striking in the ratios of the anti-B titers because of the generally lower range of anti-B levels in both media.

The difference in the maternal-fetal ratios established with the two methods of titration suggested that two separate antibodies cross the placenta, namely, a saline agglutinin and a more readily transferable "conglutinin" measurable in gum acacia. To test this hypothesis further, the relationship between the height of the saline titer and the titer in gum acacia in each individual maternal serum was compared with the same relationship in each corresponding cord blood. In the maternal sera, the gum acacia titers for anti-A were generally one or two dilutions higher than the saline titers. Only 10 of the 69 maternal sera for which the corresponding cord sera were available showed a spread of three or more tubes (Chart 2). By contrast, 59 of the 69 cord sera showed a spread of three or more tubes between the titers in saline and those in gum acacia medium, only 10 having a spread like that found in the majority of the maternal sera. This exact reversal of the maternal saline-gum acacia titer differences in the cord sera seemed beyond coincidence and indicated that the antibody measured by the acacia titration was qualitatively different from that measured as a saline agglutinin and did indeed pass the placenta

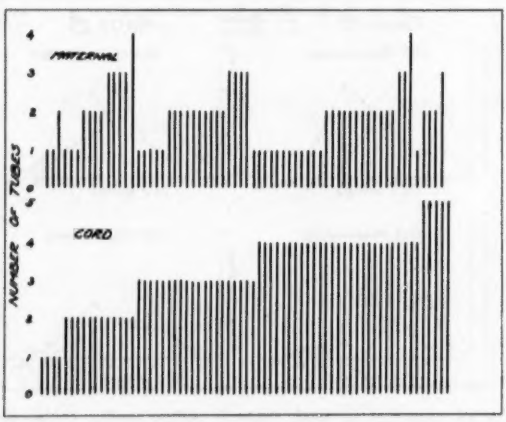

Chart 2.—Differences between saline and gum acacia titers expressed in numbers of tubes (titration units). Upper row represents the maternal sera, lower row, the cord sera, arranged in such a way that each cord is plotted under the corresponding maternal serum.

independently and more readily. Though the quantitative relationships are illustrated only for anti-A, the findings with respect to anti-B were entirely comparable. The permeability of the placenta in a given case was generally of the same order for the α as for the β antibody. This relationship could be derived from a comparison of the maternal fetal ratios for anti-A with those for anti-B and held for both saline and acacia antibody.

Heterospecific Pregnancies.—In the heterospecific pregnancies of type O-A or O-B, the pattern of the cord-blood antibodies differed from that in homospecific pregnancies chiefly in that the homologous antibody, i. e., the antibody antagonistic to the infant's own blood group was as a rule absent. There were a few exceptions, to be described presently. The demonstration of the heterologous antibody was less often successful than that of the same antibody in the cord blood of Group O infants (Table 2). By saline titration, 19, and by gum acacia titration, 3, of the cord sera of 47 Group A infants of O mothers failed to show anti-B antibody,

although the maternal anti-B titers were in the same range as the anti-B titers of Group O infants of O mothers. The sera of the 53 Group B infants showed no anti-A in saline in three instances and none in gum acacia in one of these. In this last case, the maternal serum had the unusually low anti-A titer of 1 : 16 in saline, although the titer in gum acacia was 1 : 128. Apart from the slightly larger number of cord sera which failed to show the expected antibody, the range of the cord titers in the heterospecific groups was the same as in the Group O infants.

In none of the 53 cases of Group B infants of O mothers could the homologous (anti-B) antibody be demonstrated in the cord blood by titration in either medium. Similarly, no saline or gum acacia anti-A titer was obtained in 43 of the 47 infants belonging to Blood Group A. In four cord sera of Group A infants, however, anti-A antibody was demonstrable in the gum acacia medium. Interestingly, three of these four infants belonged to subgroup A_2, whereas in the group of all A infants the proportions between A_1 and A_2 were reversed, only 20% being A_2. All of the four Group A infants whose cord blood contained anti-A were secretors. None had clinical or hematologic evidence of hemolytic disease. In the case of the three Group A_2 infants the maternal sera showed no evidence of an immune response at the

TABLE 2.—*Incidence and Range of Titers of Antibodies Found in Cord Bloods in Heterospecific Pregnancy*

	47 O-A Pregnancies				53 O-B Pregnancies			
	Anti-A		Anti-B		Anti-A		Anti-B	
	Saline	Gum Acacia	Saline	Gum Acacia	Saline	Gum Acacia	Saline	Gum Acacia
No. of cases	1	4	28	44	50	52	0	0
Range	Undil.	4-8	1-8	1-64	1-64	4-256	..	..
No titer found	46	43	19	3	3	1	..	..

time of delivery or post partum. In one instance a weak saline agglutinin was demonstrable in the cord serum along with the conglutinin.

In the single case of an A_1 infant whose cord blood contained anti-A, the initial typing had given an A_2 reaction which persisted at 3 weeks of age. Only at 5 months of age could an A_1 reaction be demonstrated. The maternal serum was described in the preceding paper as the only example of immune anti-A found at term in the group of O-A heterospecific pregnancies (Case 359). The partially neutralized serum of this mother had a titer against A of 1 : 8 in saline and 1 : 256 in serum and also activity against B cells. There were no recognizable effects of the maternal immune antibody in the infant, and there were no appreciable postpartum changes in the maternal antibody pattern.

In contrast to the homospecific O-O pregnancies in which almost invariably both anti-A and anti-B could be demonstrated in the infants and to the O-A and O-B heterospecific pregnancies in which only one, namely, the heterologous antibody, was usually found in cord sera, in the 19 mixed heterospecific pregnancies neither antibody could be found in the cord sera. Thus in the case of an A_1 baby of a B mother anti-A antibody such as was readily demonstrated in the maternal serum was never found in the cord blood.

The direct Coombs test was performed on every available cord blood from all types of pregnancies and was uniformly negative. The indirect Coombs test against

cells of the same blood group as that of the infant was performed in 28 cord bloods, Group O cells serving as controls, and was negative in 27 instances. In one case, that of a B secretor baby of an O mother, a weakly positive indirect Coombs test was obtained with adult B test cells. The maternal anti-B titers in this case were 1 : 16 in saline, 1 : 128 in gum acacia. The cord blood showed no titer against B by titration in either medium. Although there was a postpartum reaction in the mother, as shown by the appearance of marked resistance of saline β agglutinins to neutralization with soluble B substance,[1] the maternal serologic pattern at delivery was not remarkable. We have no explanation for the isolated finding of a positive Coombs test, which does not fit our general experience.

Attempts were made to elute homologous antibody which might be attached to the fetal erythrocytes. The eluate, prepared as described in the first paper, failed to agglutinate the appropriate cells in the 48 cases of A and the 42 cases of B infants of O mothers in which the test was made.

COMMENT

An understanding of the factors determining the passage of isoantibodies in homospecific pregnancy is prerequisite to the study of the effects of antibody antagonistic to the fetus in heterospecific pregnancy. When mother and fetus belong to the same blood group, the fate of maternal isoantibodies crossing the placenta cannot be influenced by fetal blood-group antigens. The fact that in homospecific pregnancy the cord serum may show the same qualitative pattern of agglutinins against A and B as does the maternal blood is well established. It seems generally agreed that the mother is the source of the antibodies found in the cord serum. The observations presented above support this assumption by demonstrating that the maternal antibody titer governs the upper limit of the fetal titer of the same antibody. The other factors which may determine the passage of isoantibodies into the fetus are not well understood, partly because of discrepancies in actual observations, partly because of theoretical disagreements concerning the nature of isoantibodies capable of passing the placental barrier.

Every student of the problem has noted considerable variation from case to case in the ratios between maternal and fetal titers. This variability was quite evident in the present series, with ratios varying from 64 : 1 to 1 : 1. Tovey [2] expressed the variable as placental inhibition. He noted that the inhibition was approximately the same for anti-A and anti-B in any given pregnancy of the type mother O, infant O. Our observations on this point agree with those of Tovey. Like this author, we found the expected complete antibody pattern of the mother in the vast majority of the cord sera. In only one case did the cord serum show neither anti-A nor anti-B saline agglutinins. In the remaining 68 cord sera of O infants, anti-A was always found and anti-B, 61 times. The absence of anti-B in a few cord sera is hardly surprising in view of the generally low maternal anti-B saline titers. The conclusion appears justified that anti-A and anti-B saline agglutinins can and usually do pass the placenta in O infants of O mothers.

Our observations and those carried out by Tovey on a smaller series of cases are in apparent disagreement with the results obtained by Wiener and his associates [3] and by the Australian authors, Jakobowicz and Bryce.[4] These authors failed to find the expected agglutinins in the cord serum in a large proportion of their cases. The explanation of the discrepancy seems to lie in a technical consideration.

In the present study, the antibodies of both mother and fetus were routinely tested against standard A_1 cells of high reactivity supplied by one and the same person and also against B cells obtained from one person. Wiener and his associates routinely used A_2 cells for the titration of anti-A. With such test cells, the titers of anti-A should be lower than with A_1 cells, and antibody of low concentration might be missed. The Australian authors did not specify the source of their test cells or indicate the subgroup of A. If, as is likely, fresh A and B cells were used as they became available from different donors, the demonstration of low-titer saline agglutinins would fail whenever cells of low reactivity were used.

The studies reported by most of the previous investigators were concerned solely with the saline agglutinins of the cord blood. Wiener and his associates introduced the gum acacia technique for the demonstration of "conglutinins" and showed that antibody was more often found with this method than with saline media. The experience obtained in the present series is in agreement with Wiener's findings. In gum acacia medium anti-A as well as anti-B was virtually always found in the cord sera of Group O infants of O mothers, even if saline agglutinins could not be demonstrated. The placenta must therefore be permeable to some degree to anti-A and anti-B in almost every pregnancy.

Theoretical disagreement exists concerning the kind of antibody which can pass the placenta. Wiener and his associates [3] proposed the theory that only "univalent" antibodies, i. e., the antibodies demonstrated as conglutinins by the gum acacia technique, could enter the fetus, while the bivalent saline agglutinins were held back by the placental barrier. They based this theory on their failure to find appreciable titers of saline agglutinins in cord sera and assumed that such activity as could be demonstrated in saline media was due to conglutinins rendered active by the presence of sufficient colloid to produce a visible agglutination. As mentioned above, the low titers obtained by these authors must be attributed largely to their use of A_2 test cells. The often substantial saline agglutinin titers found in the present series can hardly be interpreted as conglutinin effects. Our data, rather, seem to indicate the normal existence of two separate antibodies which can both pass the placenta and do so independently, one measured by titration in saline, the other in a colloid medium. As shown by the generally much lower maternal-fetal ratios of the titers in gum acacia, the "univalent" antibody is more readily transferred across the placenta than the "bivalent" saline agglutinin. The existence of two antibodies would be inferred from this difference in the ratios. More conclusive is the fact that in the cord sera the difference between the gum acacia and the saline titer for either antibody was variable and as a rule greater than the difference of the simultaneously studied maternal titers. If only one kind of antibody, the "conglutinin," were capable of crossing the placenta and, accidentally as it were, giving weak reactions in saline media, the difference between gum acacia and saline titer in the cord sera would be fixed, and only very low titers would be observed.

More significant than the relationship between conglutinins and agglutinins is the fact that both anti-A and anti-B pass the placental barrier in some form in the overwhelming majority of pregnancies of the type mother O, infant O. It follows that in heterospecific pregnancy, mother O, infant A or B, both maternal isoantibodies must also pass the placental barrier, the antibody antagonistic to the fetal blood group as well as the antibody which has no effect on the fetal group. The neutral antibody could be demonstrated in the cord serum in heterospecific preg-

nancy with almost the same frequency as the same antibody in Group O cord sera. It is difficult to conceive of a mechanism which would specifically retain one but not the other antibody at the endothelial barrier, depending on the blood group of the fetus. The absence of the antagonistic antibody in most A or B cord sera, therefore, indicates that it is neutralized after crossing the placenta. The neutralization might be accomplished in placental tissues, fetal tissues, erythrocytes, body fluids, or a combination of any of these. The secretor status of the fetus seems to have no significance for the neutralization of anti-A or anti-B, since both secretors and nonsecretors have ample A or B substance in their organs and tissues. This point is proved by the observations showing absence of antibody antagonistic to the fetal blood group in the cord sera of nonsecretors as well as of secretors.

Complete neutralization of the ordinarily occurring maternal antibodies by fetal tissue antigens of A or B specificity may therefore be assumed to be the chief mechanism effective in protecting the fetal erythrocytes. In the large majority of heterospecific pregnancies, this neutralization is accomplished, as judged by the absence of free antibody in the cord serum, and the fetus and newborn infant escape recognizable effects caused by maternal antibody. Failure of neutralization by group-specific substances should leave the antagonistic antibody free to act on the erythrocytes of the fetus. The degree of hemolysis which may result might be influenced by quantitative factors, such as the amount of antibody reaching the fetus and the amount of tissue antigens capable of absorbing it. Qualitative factors, such as the "fit" between antibody and antigen, might also be involved. These relationships will be examined more closely in the section dealing with pathologic variants of heterospecific pregnancy. Here it is necessary to refer to them because of the observation that free antibody antagonistic to the fetal blood group is not invariably associated with demonstrable hemolysis. A hemolytic process was not demonstrable in 4 infants among 137 cases of heterospecific pregnancy, studied by Jakobowicz and Bryce,[4] in whose cord sera the unexpected antibody was found as saline agglutinin. Wiener and his associates encountered very weak conglutinins effective against A in the cord serum in four of six O-A heterospecific pregnancies with normal infants and conglutinins against B in two normal Group B infants. In the present series no anti-B was demonstrable as either saline agglutinins or conglutinin in the sera of Group B infants. Anti-A, however, was present in 4 of the 52 cord sera of Group A infants born to O mothers. All four infants were secretors, and all appeared entirely normal. In one case the maternal serum had "immune" characteristics, but in the other three cases the maternal sera showed no unusual features. All four of the infants' bloods gave A_2 reactions at birth, though later one, that of the infant whose mother had "immune" anti-A, developed into A_1. The other three infants were still A_2 at the age of 6 months. In the group of A infants as a whole the proportions of A_2 to A_1 were exactly reversed. It seems likely that the maternal anti-A in the four infants was essentially an antibody of A_1 specificity which failed to be adequately neutralized by the A_2 (or the single A_1 behaving like A_2 at birth) of the fetal tissues. For the same reason it should fail to react with the fetal erythrocytes and thus behave like heterologous antibody, such as anti-B in an A fetus. Witebsky * has expressed the same view regarding the occurrence of

* Witebsky, E.: Personal communication to the authors.

anti-A in the sera of normal A infants. The low reactivity of the fetal erythrocytes in some instances seems to provide additional protection against harmful effects of maternal isoantibodies.

The observed facts fit the following interpretation of the immunologic events in O-A and O-B heterospecific pregnancy with normal outcome. Both maternal isoantibodies, anti-A and anti-B, pass the placental barrier whether they happen to be antagonistic to the fetal blood group or not. The placental permeability varies from case to case but is approximately the same for anti-A as for anti-B. There are at least two kinds of antibody which are capable of passing the placenta independently, saline agglutinins as well as conglutinins, or univalent antibodies. In the fetal or placental tissues the antagonistic antibody, whether agglutinin or conglutinin, is neutralized by group-specific substances known to be present in both secretors and nonsecretors. The presence of water-soluble group-specific substances in the body fluids of the secretor infants does not add to this protective mechanism. The significance of the secretor status lies solely in the ability of soluble substances reaching the maternal circulation at delivery to evoke immune responses post partum.[1] Free antibody found in the cord serum is antibody which has not been neutralized. It may be tolerated in normal infants in whom such a failure of neutralization appears to be a qualitative phenomenon related to the low reactivity of fetal A_2 cells (and perhaps occasionally A_1 cells with initial A_2-like reactions). The differences between cases of heterospecific pregnancy in which the infants are fully protected and those in which they show harmful effects of maternal anti-A or anti-B will be fully discussed in a later communication.

The differences between Rh and ABO heterospecific pregnancy are marked in several respects:

1. Anti-A or anti-B antibody is normally present in the maternal serum and normally reaches the fetus. Rh antibody is never normal in either maternal serum or in the fetus.

2. Anti-A and anti-B saline agglutinins, as well as univalent antibodies, can pass the placenta, whereas the evidence is overwhelming that saline Rh antibodies cannot do so.

3. The fetal tissues of both secretors and nonsecretors contain sufficient A or B substance to neutralize the ordinary anti-A and anti-B antibodies, though in this respect there seems to be a difference between A_1 and A_2. Rh antibodies are not neutralized by tissue substances; hence the presence of antibody in the fetus produces hemolysis.

SUMMARY

The isoantibody patterns of cord sera were compared with those of the corresponding maternal sera in homospecific and heterospecific pregnancy. In homospecific pregnancy mother Group O, infant Group O, both anti-A and anti-B antibodies were demonstrated in the vast majority of cord sera. Evidence was presented that in this type of pregnancy both saline agglutinins and "conglutinins" of anti-A and anti-B specificity pass the placental barrier. The height of the fetal titer was limited by that of the maternal titer but in addition was influenced by an individual variable of placental permeability. The saline agglutinins were found to pass the placenta less readily but independently of the conglutinins.

In contrast to homospecific pregnancies where the maternal antibody pattern is nearly always completely represented in the cord serum, in heterospecific pregnancy type O-A or O-B the antibody antagonistic to the fetal blood group was nearly always absent from the cord serum. The heterologous antibody was found in the cord sera of this group with nearly the same frequency as in homospecific pregnancy. In heterospecific pregnancy of Type A-B or B-A the single isoantibody present in the mother and antagonistic to the fetal blood group was regularly absent. These facts were interpreted as evidence that the placenta is normally permeable to maternal isoantibodies against A and B, whether or not they affect the fetal blood group. The mechanism chiefly responsible for the protection of normal infants in heterospecific pregnancy appears to be the neutralization of the potentially harmful maternal antibody by A or B substances in the tissues of the fetus. No evidence was found that the secretor property added to the degree of protection. In some cases free anti-A antibody was found in the cord blood of apparently normal infants of Blood Group A. Since in all instances the blood of these infants gave the reactions of Subgroup A_2, the hypothesis was advanced that the maternal antibody reaching the fetus had A_1 specificity and behaved essentially like a neutral antibody.

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CYSTIC LYMPHANGIOMA OF THE LOWER EXTREMITY

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ALTHOUGH cystic hygroma of the neck is not a common lesion, the occurrence of a similar tumor in the thigh is still much more infrequent. In a 5-year-old child, we encountered a swelling of the upper leg with the characteristics of a cystic lymphangioma. This case is of further interest because the patient was observed from the age of 5 to 13 years, when a third operation was indicated to remove residual tumor.

REPORT OF A CASE

R. P., a 5-year-old boy, was first admitted to the Presbyterian Hospital on June 21, 1945, for surgical excision of a mass of the right lower extremity. The mother stated that this tumor had been present since birth and that it had varied in size and consistency, on some occasions being soft, while at other times there was marked distention of the thigh in the region of the swelling. There was purplish-blue discoloration of the hip subsequent to a fall. The child was otherwise in good health.

The general physical examination was negative, except for the outer side of the right hip and the inner side of the right upper leg, where there was a soft mass extending from the region of the right iliac crest down to within a few centimeters of the patella. The mass followed the course of the sartorius and adductor muscles (Fig. 1). The skin over the upper half of this lesion was tense and discolored; yet there was no apparent dimpling. No infection was present. The child did not have a limp.

Laboratory Examinations.—The laboratory findings were as follows: blood—hemoglobin, 12 gm.; RBC, 3,980,000; WBC, 9,950; differential white cell count, normal; urine, negative for albumin, sugar, and cells. Roentgenograms of the pelvis and upper end of the femur showed no evidence of bone changes. There was, however, a soft-tissue swelling lateral to the greater trochanter of the right femur.

At operation on June 25, 1945, a semilunar incision was made over the outer aspect of the right thigh. Subcutaneous exploration resulted in the removal of a large block of tumor tissue, which was composed of masses of fibrous connective tissue in which there were interlacing smooth-lined channels filled with a clear watery fluid. Only a portion of the tumor was removed at this time, as the dissection was quite vascular. A subcutaneous drain was left in place. Blood transfusions were administered on two occasions without reaction. The postoperative course was uneventful.

On Oct. 9, 1946, the patient returned to the Presbyterian Hospital. The remaining tumor, which lay over the adductor and sartorius muscle groups of the right thigh, was excised through a medial longitudinal incision. At this time it was thought that all the tumor had been removed. A pressure dressing was applied. The postoperative course was without incident. The child was discharged Oct. 23, 1946.

On Sept. 16, 1952, the patient, now 12 years of age, returned with the complaint of pain just above the right patella. Here there was a firm subcutaneous irregular mass approximately 4 by 6 cm., which was slightly movable. The skin was smooth, the color normal. It was thought that the painful swelling was probably residual lymphangioma.

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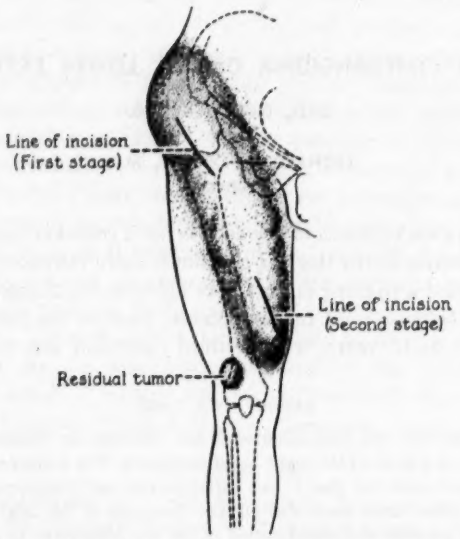

Fig. 1.—Artist's sketch illustrating the degree of involvement of the right thigh by cystic lymphagioma.

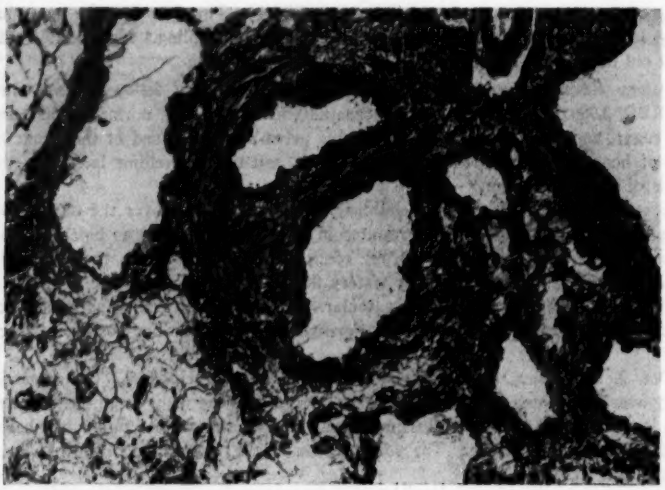

Fig. 2.—Photomicrograph of tumor removed at the first operation, showing dilated spaces lined by endothelial-like cells.

Through a small semilunar incision, a block of subcutaneous tissue was removed, which grossly and histologically resembled the cystic changes seen at the previous operations (Figs. 2 and 3). The patient was discharged on Sept. 21, 1952, with primary healing of the wound. There had been no limitation of function of the extremity. The boy is as active in athletic games as his playmates. No residual tumor is apparent to date.

COMMENT

Numerous reports have appeared in the surgical literature on cystic hygroma of the neck, but few are concerned with the presence of cystic lymphangioma located elsewhere in the body. Ward, Hendrick, and Chambers [13] state that although 93% of the reported cases of cystic hygroma occur in the neck, such tumors are also found in the axilla, mediastinum, popliteal fossa, groin, and/or the retroperitoneal space.

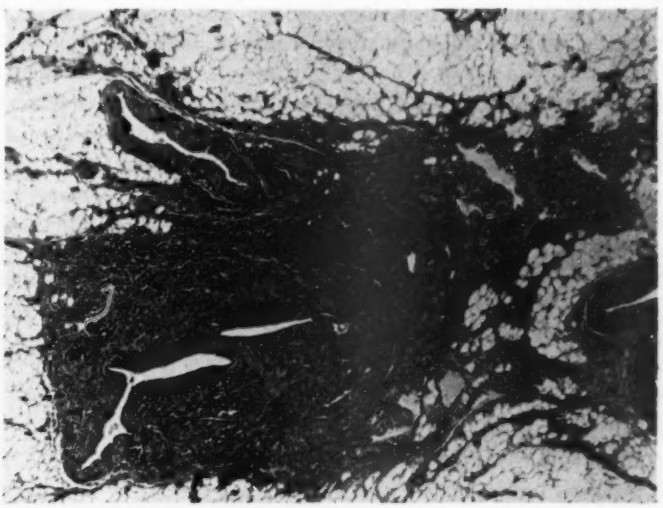

Fig. 3.—Photomicrograph of the residual tumor found at the third operation. Note the elongated cystic spaces surrounded by dense fibrous connective tissue. This specimen was similar to those removed at the earlier operations.

Many authors have made contributions to the knowledge of cystic hygroma, the first being Wernher,[14] in 1893. He believed that lymphangioma was a new formation independent of the development of the fetus. Other theories are held as to the cause of cystic lymphangiomas, namely, that these lesions develop from the simple modification of preexisting lymphatic structures or are the result of varicosities of lymphatic vessels, with secondary cystic degeneration, or originate as true neoplasms caused by the proliferation of embryonic cell rests.

Sabin's [10] work on the normal development of the lymphatic system affords a basis for understanding the formation of cystic hygroma. McClure and Silvester [7] made comparative anatomic studies of the development of the lymphatic system and indicated the relationship of that system to the venous circulation.

According to Goetsch,[5] the plausible theory is that cystic hygroma arises from sequestrations of lymphatic tissue. In cases of cervical hygroma, such sequestrations

are derived from the primary jugular sacs which have failed to join the lymphatic system in the normal manner. Their potentiality of increasing in size to an almost unlimited extent is due to the fact that these "lymphatic rests" retain their embryonic power of irregular growth. In an excellent review of the etiology and pathogenesis of cystic hygroma, Goetsch showed from histological material that cystic hygromas arise primarily by the formation of endothelial fibrillar membranous sprouts derived from the walls of cystic spaces already present. These sprouts penetrate the neighboring normal tissues, eventually become canalized, and form other cysts. In addition to demonstrating the manner of growth, he emphasized the tendency of these lesions to penetrate and destroy surrounding structures.

Vaughn [12] compiled a series of 64 cases of cystic hygroma from the literature, in addition to Dowd's report of 91 cases up to 1914. He operated successfully on an infant 2 months of age who had a huge cystic hygroma the size of a newborn infant's head. He pointed out that true cystic hygroma of the neck is rare but that cystic lymphangiomas are still more infrequent in the axilla, arm, or chest, over the sacrum, or in the groin or leg. These lesions are often observed at birth but may escape diagnosis until later in life. Some authors have reported a higher incidence of these tumors in females than in males.

These tumors are soft or spongy, vary in size and shape, and contain cystic spaces filled with clear watery fluid. Previous infection in the tumor may cause induration of the lesion and surrounding tissues. The skin is often smooth and under tension; yet it may be puckered and attached to the lesion. If there is a history of recent trauma with hemorrhage, these lesions may appear blue or purple. Goetsch states that the marginal cysts penetrate and destroy large areas of adjoining muscle and may infiltrate and penetrate nerve sheaths as well as blood vessels. The pressure of a large tumor on the trachea may produce obstruction to respiration, particularly when the head is rotated.

Reichert [9] has indicated that the benign type of lymphangioma is soft, is slowly growing, has only a moderate tendency to invade surrounding tissues, and resists infection, whereas the malignant type is tense, has periods of rapid growth, has great power of penetration, and shows a tendency to become infected. In this latter group, he suggests that the result of surgical intervention is unpredictable because of the impossibility of complete removal of the tumor without a limiting capsule and with wide ramifications. Although the lesion removed in the case reported here did not follow a malignant course, nevertheless, there was no distinct capsule or limiting membrane for complete isolation of the boundaries. This fact resulted in a third operative procedure, with removal of residual tumor.

Numerous forms of treatment of cystic lymphangioma have been recommended. Callister [1] quotes Baumgartner as stating that complete removal is usually an absolute impossibility because these lesions have invasive properties into any and all surrounding structures. This fact, associated with a high susceptibility to infection, results in a rather high mortality.

Figi,[3] of the Mayo Clinic, in 1929, reported that radium therapy alone was adequate in the treatment of cystic hygroma; however, the mortality rate was high in the cases reported due to infection. Harrower [6] suggested injection of a sclerosing solution, as sodium morrhuate, to reduce the size of the lesion and to stimulate a

fibrous tissue reaction which would result in obliteration of the disease process. Ward and his associates suggested aspiration of the cyst contents and immediate injection of a sclerosing solution, followed in three to six weeks by complete surgical extirpation. With this plan of treatment, reported in 20 consecutive cases observed in 10 years, there were no recurrences and no operative fatalities. Preliminary incision and drainage of cystic lymphangioma has been advocated but this form of treatment alone is inadequate and may introduce secondary infection, which in instances reported in the past has resulted in high mortality. With the antibiotics available, the incidence of infection is, of course, greatly lessened.

Goetsch has recommended early radical surgical removal, but has suggested the use of radiation for older children if the lesion is unusually large, making radical excision too hazardous. In most cases, radical surgical treatment is preferred over roentgen therapy.

Ravitch [8] advocated and performed radical operative procedures with apparent cure in three cases of massive tumor composed of a mixture of cystic hygroma, hemangioma, and cavernous telangiectatic lymphangioma. Freeman [4] recently reviewed a series of cases in which he suggested conservative surgical procedures in the treatment of cases with massive lymphangioma. His follow-up results were excellent. He fails to agree with Ravitch that radical surgery is necessary in the management of these cases.

Sawyer and Woodruff [11] advocated surgical removal in a series of eight cases operated upon successfully. They emphasized the importance of early recognition and prompt removal of the lesions to prevent complications or recurrence.

Early complete surgical excision is the treatment of choice of cystic lymphangioma in most instances. With improved surgical techniques and anesthesia, replacement of large quantities of whole blood, and the availability of penicillin, streptomycin, and other antibiotics, surgical attack on these extensive lesions is indicated.

SUMMARY

The case is presented of a 13-year-old boy who was seen first at the age of 5 years. He had a large cystic lymphangioma of the right lower extremity, which involved the thigh and extended down the inner aspect of the upper leg along the course of the adductor and sartorius muscle groups. Two separate operative procedures were required to remove the major portion of the tumor. A third operation resulted in the removal of residual cystic tumor located above the patella. At the present time, there is no evidence of recurrence. There is no limitation of function of the extremity, as the boy is engaged in the usual physical activities of a child in this age group.

Total surgical extirpation of these cystic lymphangiomas is advocated, preferably early in life. Careful attention to preoperative preparation is urged. This type of treatment is possible as long as adequate anesthesia and proper blood replacement are available. The administration of the antibiotics in these cases has markedly reduced the incidence of infection. One should remember that the dissection is often long and vascular.

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NEUROTOXIC SYMPTOMS FOLLOWING INGESTION OF ASTEROL DIHYDROCHLORIDE

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THROUGH communication with Hoffmann-LaRoche, Inc., manufacturers of the antifungal drug Asterol (2-dimethylamino-6-[β diethylaminoethoxy]-benzothiazole) dihydrochloride, it was ascertained that there have been reported cases of Asterol intoxication consisting of neurotoxic symptoms due to absorption from topical applications. We believe we have the first case of neurotoxic symptoms in an infant that can be attributed to ingestion of Asterol.

REPORT OF A CASE

H. G., a white boy, aged 7 weeks, was admitted to the hospital on Sept. 9, 1953, with the history of convulsive seizures first occurring on the day of admission. The first seizure occurred at 7 a. m. while the patient was being breast-fed. It consisted of marked muscle tremors of his left eye, cheek, arm, side, and leg. The duration was approximately three minutes. The patient was examined by one of us (C. H. G.) in his office, where two seizures were observed. These involved the right side, and a lateral nystagmus was noted. He was then admitted to the hospital for treatment. Between 7 a. m. and admission to the hospital at 3 p. m. of the same day, the patient had seven seizures simi'ar to the first, of which all but the first were on the right side. Between the seizures, he had seemed drowsier than usual, but otherwise he was all right.

Further history disclosed that the patient had been a full-term normal uncomplicated hospital delivery. The birth weight was 7 lb. 2 oz. (3,232 gm.). He was breast-fed and was given 10 drops of a multiple vitamin preparation daily. He had been gaining weight and had been well until the convulsions occurred. His temperature was normal on the first morning of his illness. There was no history of trauma. The mother's twin brother had had two "convulsions" during infancy but had remained well since then. Three days prior to admission, the mother had inadvertently substituted 10 drops of 5% Asterol dihydrochloride for his vitamin drops. This was given to him at 9 a. m. in 1½ to 2 oz. (5.6 to 7.3 cc.) of orange juice. That day he seemed fretful but continued taking his feedings well. There was no change in the color or quantity of the urine or of the stools. There was no vomiting.

The physical examination on admission disclosed a normal healthy infant weighing 10 lb. 8 oz. (4,763 gm.), with a rectal temperature of 98 F. Neurological examination gave normal results.

Laboratory examinations revealed a normal urine. The erythrocyte count was 3,400,000, with 9.2 gm. per 100 cc., or 63%, HgB. The total leucocyte count was 10,350, with 53% segmented cells, 1% stab cells, 41% lymphocytes, 1% eosinophiles, and 4% monocytes. A lumbar puncture was traumatic, and the cerebrospinal fluid was grossly bloody, with a total leucocyte count of 34 per cubic millimeter, with 40% neutrophiles, 60% lymphocytes, and an erythrocyte count of 80,000 per cubic millimeter, of which 95% were fresh cells and 5% were crenated. The total protein was 142 mg. per 100 cc., with a positive globulin. The cerebrospinal fluid was under no increased pressure. Roentgenograms of the skull were normal.

In the 24 hours following admission, he had seven more convulsions of two to seven minutes' duration. One was generalized; the others were predominantly right-sided. There was marked tremor and twitching of the right eyelid, cheek, mouth, right arm and hand, right side, and right leg. There was no cyanosis. There was a lateral nystagmus. He appeared to be all right in the intervals between convulsions, except that he kept both eyes turned to the left. He could be made to look straight ahead but could not be made to look to the right. When he looked straight ahead, there was slight deviation of the right eye medially. There was no anisocoria, and the pupils reacted to light. The ophthalmoscopic examination was not satisfactorily accomplished.

The seizures usually occurred when the mother tried to feed the patient at breast and his fluid intake was low; consequently he was given 350 cc. of fluids parenterally on the day after admission. Small doses of phenobarbital for sedation were given because the convulsions continued and were more frequent.

During the next 18 hours, there were no more seizures, even when he was handled for feeding. There was no change in the appearance of the eyes, but he was discharged to be watched at home. At the time of the follow-up visits two weeks and then one month later, he had had no further seizures; the eyes had returned to normal, and the patient was asymptomatic. The mother continues to feed the baby at breast. He was normal on physical examination and had gained weight.

COMMENT

Although it was not definitely proved that this patient's convulsions were due to intoxication from Asterol ingestion, no other explanation was found during the study of the patient. Because of the reported cases of convulsions in infants and children following topical application of Asterol, we have assumed that Asterol dihydrochloride was the causative agent in this patient's convulsions. It is recommended that the directions on the label of the product to refrain from using it in infants and small children be closely followed.

Doctors Building (Dr. Gay).

Case Reports

CYSTIC TUBERCULOSIS OF THE BONES IN CHILDREN

Report of Two Cases

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TUBERCULOSIS of the long bones in children usually attacks the metaphysis, with early caseation and abscess formation. Less commonly, single or multiple tuberculous foci are found in the diaphyses, with localized thinning of the cortex and formation of cyst-like structures. These tuberculous cysts may remain stationary for long periods, may progress to abscess formation, or, more frequently, may heal without complication. Such cyst-like areas in roentgenograms of the long bones, especially when unaccompanied by sinus or abscess formation, may present problems in differential diagnosis. For this reason, we present the following two cases of cystic tuberculosis of the bones.

REPORT OF CASES

CASE 1.—B. T., an 18-month-old Negro girl, was admitted to the Pediatric Clinic of Provident Hospital (Chicago) on Jan. 27, 1938, with the complaint of disability in the region of the left shoulder.

Past History.—The child was born at term of a normal spontaneous delivery. The birth weight was 7 lb. (3,175 gm.). She was breast-fed for 10 months and received orange juice and cod liver oil regularly from the age of 1 month. Her neuromuscular development was normal, and her past medical history was uneventful, except for an attack of uncomplicated varicella one month prior to admission.

One week prior to admission, the mother noted a slight swelling and mild tenderness at the proximal end of the left arm. The child refused to use the affected member and cried when passive movements were attempted. There was no history of trauma.

The mother, aged 24, was in good health. Her blood Wassermann was negative, and a roentgenogram of her chest showed nothing significant. The father was not available for examination. The only sibling, a 3½-year-old girl, was apparently well, but had a positive tuberculin reaction. The children had been in direct contact with a maternal uncle who had recently been admitted to a sanitorium for the treatment of pulmonary tuberculosis.

Physical Examination.—The patient (Fig. 1) was a well-developed somewhat poorly nourished child weighing 22 lb. (9,980 gm.) and measuring 32 in. (81 cm.) in length. The temperature was normal, and the child did not appear ill. There was pallor of the skin and mucous membranes. Examination of the eyes, ears, nose, and mouth revealed nothing abnormal. The anterior cervical lymph nodes were enlarged and shotty. The heart, lungs, spine, and

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abdomen gave negative findings. The extremities were normal, except for the left shoulder, which presented redness, tenderness, and slight swelling of the soft tissues on the anterior and superior aspects. The child carried the arm limp at her side and resisted all passive movements. However, when urged, she would use the arm to a limited extent.

Laboratory Findings.—The laboratory findings were as follows: hemoglobin 11.2 gm. (Sahli); RBC 3,600,000; WBC 7,550; differential, neutrophiles 61%, lymphocytes 37%, eosinophiles 2%. No abnormalities were noted on the blood smear. Blood Wassermann and Kahn tests were negative. The urine was normal. Blood calcium was 10.1 mg. per 100 cc.; phosphorus, 5.4 mg. per 100 cc. An intracutaneous tuberculin test (0.1 mg. old tuberculin [OT]) was strongly positive.

Fig. 1 (Case 1).—Photograph of patient, showing pointing mass in left anterior axillary fold.

Roentgenographic Findings.—Roentgenograms of the entire skeleton were negative, except for the left humerus. The first examination (Jan. 27, 1938) revealed expansion of the proximal third of the humerus, which was the site of a localized multilocular cystic lesion measuring approximately 2.5 cm. by 4 cm. (Fig. 2*A*). Except for the walls of the loculi, the entire region was of decreased density. The involved cortices were thinned, and there was a pathological fracture through the medial aspect of the cortex distal to the epiphysis. The periosteum was slightly elevated, and there was evidence of subperiosteal new-bone formation. The epiphysis appeared to be somewhat displaced from the parent bone. The lower half of the humerus was normal in appearance. Roentgenographic examination of the chest showed hilar infiltrations, which were interpreted as minimal tuberculous lymphadenopathy with beginning calcification. There was no evidence of parenchymal pulmonary lesion.

Clinical Course.—The condition of the child remained unchanged until Feb. 21, 1938, when a fairly large mass was noted in the left anterior axillary fold (Fig. 1). This proved to be a

circumscribed abscess and was surgically drained. A slowly granulating sinus tract developed at the point of incision. Two guinea pigs were inoculated with the material from the abscess, and both developed tuberculosis.

The patient at no time had fever or other constitutional signs, except for the loss of ½ lb. (230 gm.) of weight during the development of the abscess.

Treatment consisted of immobilization of the arm, dietotherapy, and ultraviolet radiation. The child responded very well to this program, as evidenced by improved appetite, gain in weight, and resumption of function in the affected part. By June, 1938, the axillary abscess had

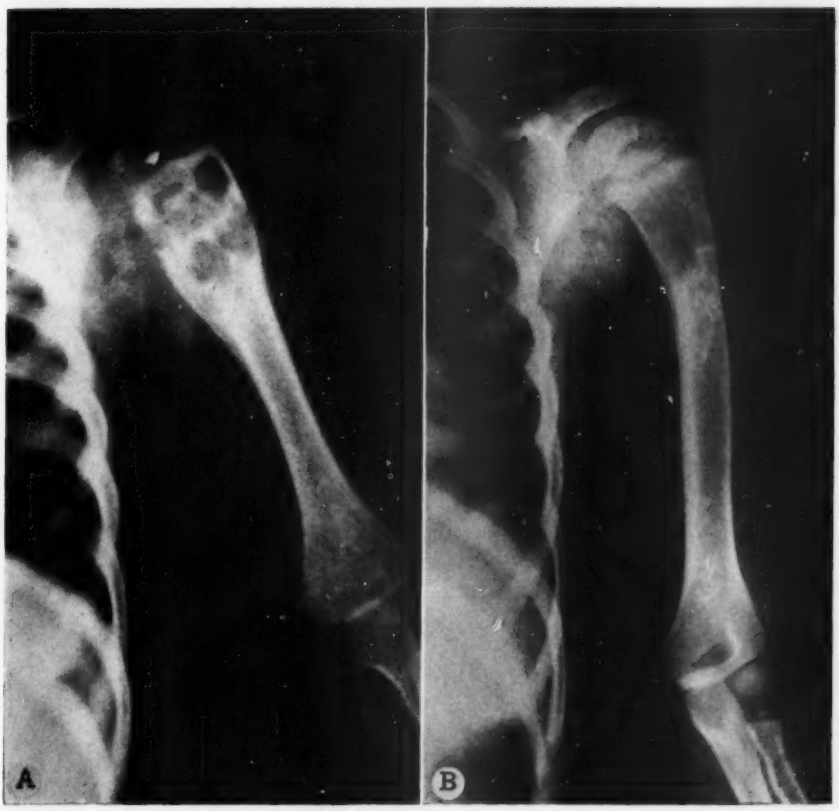

Fig. 2 (Case 1).—Roentgenograms of left humerus. *A*, multilocular cystic lesions, in January, 1938. *B*, almost complete healing, in November, 1938.

healed, and the roentgenogram showed almost complete disappearance of the cyst-like structures. A roentgenogram taken Nov. 16, 1938 (Fig. *2B*), showed further healing of the diaphyseal tuberculosis and the pathological fracture of the left humerus.

CASE 2.—R. C., a 22-month-old Negro boy, was admitted to the Pediatric Service of Freedmen's Hospital on Feb. 13, 1952, because of weakness and weight loss of three months' duration and swellings of the forehead and extremities of six months' duration.

Past History.—Birth history was not known. The child was placed in a foster home at the age of 4 weeks, weighing at that time 5 lb. 3 oz. (2,350 gm.). Neuromuscular development was apparently normal until a few months before admission. In November, 1950, he was hos-

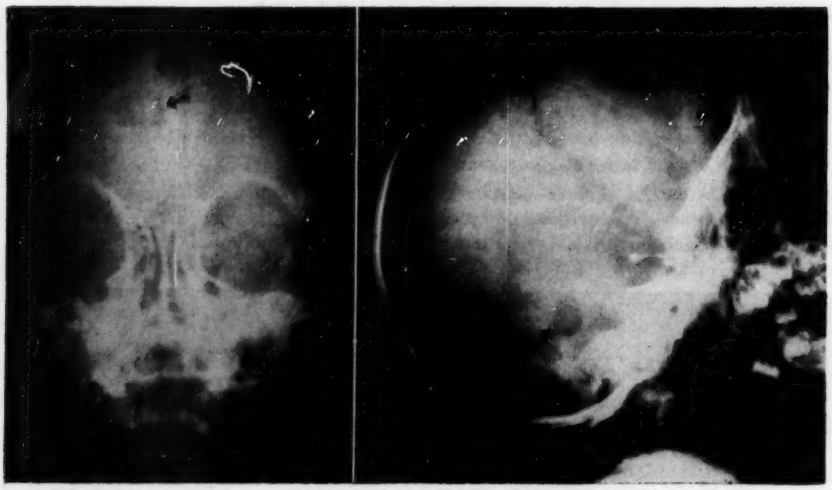

Fig. 3 (Case 2).—Roentgenograms of skull, showing osteolytic lesions of frontal and occipital bones.

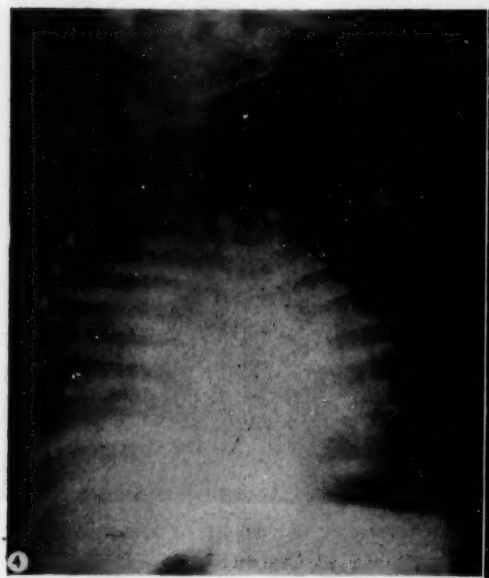

Fig. 4 (Case 2).—Roentgenogram of chest, showing massive exudation in right lung and moderate infiltration of upper left lung.

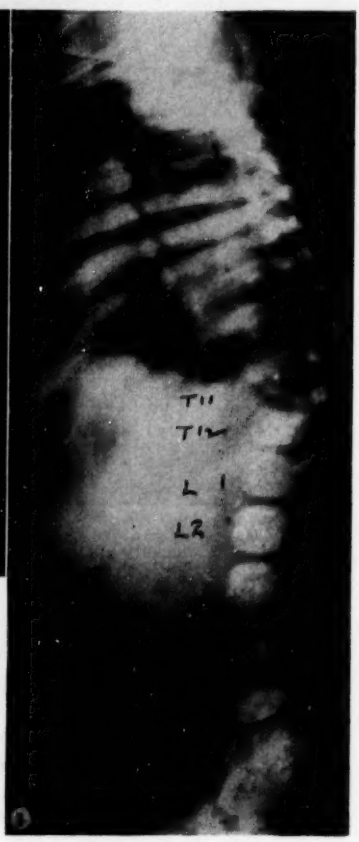

Fig. 5 (Case 2).—Roentgenogram of spine, showing disease of bodies of the 9th, 10th, 11th, and 12th thoracic levels.

pitalized for one week in another institution for bronchopneumonia. In July, 1951, he was hospitalized elsewhere for 10 days with a diagnosis of acute dacryocystitis. We have no knowledge of his tuberculin reaction prior to admission.

Six months prior to admission, a swelling had appeared on the forehead followed by swelling of the left elbow, left wrist, and lateral aspect of the left foot. In the three months before admission, he appeared chronically ill, lost weight and strength, and refused to stand or sit.

Family history was not known. He was given up by his mother shortly after birth. There was no history of contact with tuberculosis.

Physical Examination.—The patient was a chronically ill emaciated Negro boy, with marked pallor of the skin and mucous membranes. He lay in his crib and screamed out in protest when examination was attempted. The weight was 18 lb. (8,165 gm.). Rectal temperature was 100.4 F. Respirations were rapid and regular at 50 to 60 per minute, and the pulse was regular at 98 per minute.

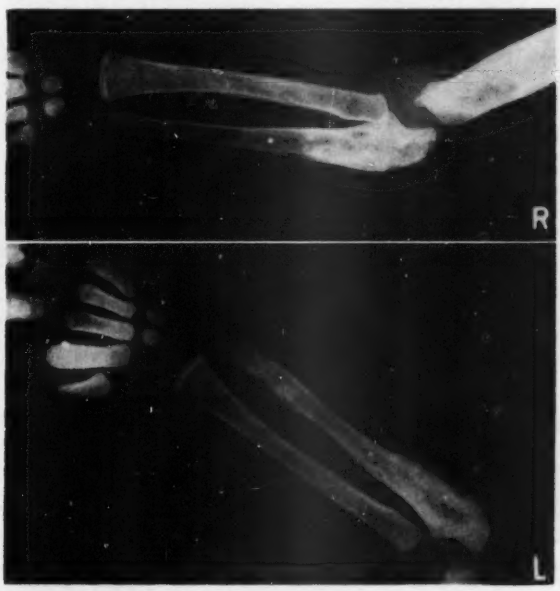

Fig. 6 (Case 2).—Roentgenograms of upper extremities, showing cyst-like areas of right humerus and both ulnas and ossifying periostitis of the distal third of the left ulna.

There were two small (1.5 cm.) cystic swellings over the frontal area. The base of the nose was flattened, with increased distance between the eyes, suggesting hyperteleorism. The anterior fontanel admitted the tip of a finger. The eyes were large and prominent. The upper lids were edematous. There was generalized lymph-node enlargement. Marked kyphosis of the dorsal spine was present. The percussion note was dull, and breath sounds were absent over the entire left lung field. The liver and spleen were moderately enlarged. The extremities were thin, with prominent joints, and were held in flexion. There was a large swelling over the left elbow and one over the lateral aspect of the left wrist. These areas were hard and appeared fixed to the underlying bone. Just above the right elbow medially was a soft-tissue mass about 1 cm. in diameter, firm, freely movable, and nontender. Over the left foot laterally, just below the ankle, was a cystic mass the size of a plum. The overlying skin was scaly, red, and shiny.

Laboratory Findings.—The laboratory findings were as follows: hemoglobin 6 gm. (42.2%); hematocrit 27; RBC 3,300,000, the majority of which were microcytes; WBC 28,450; dif-

ferential, neutrophiles 52%, large lymphocytes 23%, small lymphocytes 12%, monocytes 12%, and eosinophiles 1%. The urinalysis was negative. Serological test for syphilis was negative. Blood nonprotein nitrogen was 25 mg. per 100 cc.; blood glucose, 71 mg. per 100 cc.; blood calcium, 9.85 mg. per 100 cc. Alkaline phosphatase 5.65 Bodansky units. Total serum protein 5.75 gm., with an albumin/globulin ratio of 0.84.

A bone-marrow specimen was obtained from the iliac crest, which showed hypercellular marrow without maturation defect. Marrow smears were negative for tubercle bacilli.

The Vollmer tuberculin patch test gave equivocal results. The first-strength purified protein derivative (PPD) skin test was negative, while the second-strength was markedly positive.

The soft-tissue mass in the right arm was removed, and the pathologist reported a tuberculous lymph node.

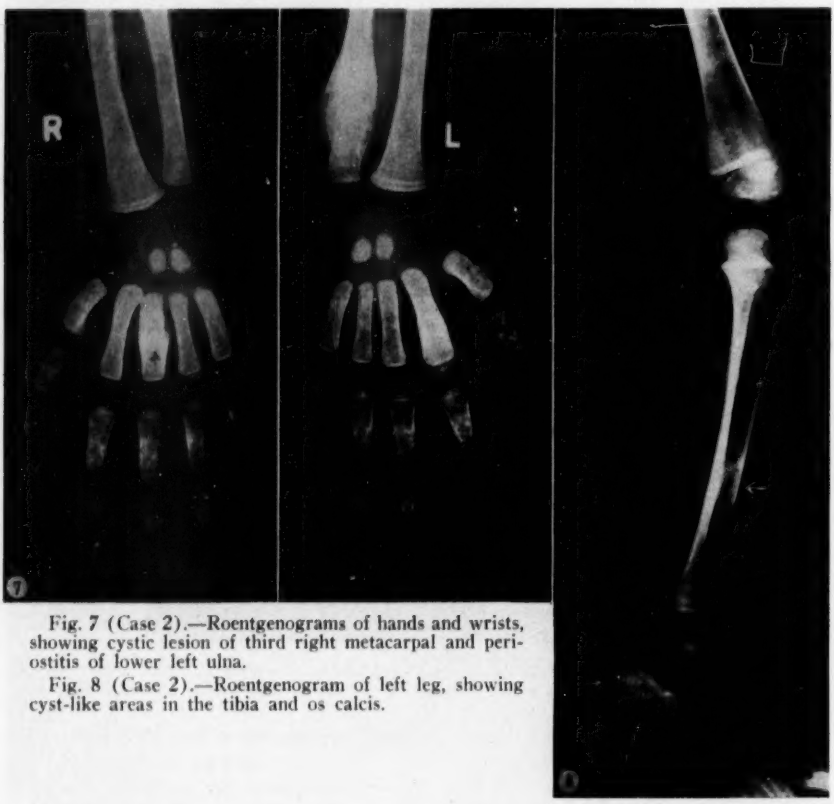

Fig. 7 (Case 2).—Roentgenograms of hands and wrists, showing cystic lesion of third right metacarpal and periostitis of lower left ulna.

Fig. 8 (Case 2).—Roentgenogram of left leg, showing cyst-like areas in the tibia and os calcis.

A biopsy of the left ulna revealed a large caseous abscess. Smear and culture of the abscess contents were negative for acid-fast organisms. The pathological diagnosis on the bone biopsy was tuberculous osteitis.

Tubercle bacilli were found on culture of the gastric washings on one occasion.

Roentgenographic Findings.—Skull: Well-defined rounded osteolytic lesions were seen in the frontal and occipital bones, measuring 1.5 to 2 cm. in diameter (Fig. 3).

The lesions were clean-cut, with no bony reaction at the periphery.

Chest: Massive exudation filled most of the right chest, with moderate infiltration of the upper left chest (Fig. 4). Cavitation was not seen. It was impossible to accurately outline the size of the heart. The trachea was deviated to the right.

Thoracolumbar Spine: Disease of the bodies of the 9th, 10th, 11th, and 12th thoracic levels, with collapse of the 10th and 11th, was present (Fig. 5).

Upper Extremities: Multiple cyst-like areas were seen involving the humerus on both sides, as well as ulna and radius. Similar changes were seen in the third right metacarpal bone. The lower left ulna showed ossifying periostitis (Figs. 6 and 7).

Lower Extremities and Foot: These films showed similar cyst-like changes in the femurs, tibias, and fibulas and the os calcis on the left (Fig. 8).

Clinical Course.—The patient was given several transfusions, with correction of anemia but very little improvement in the general clinical condition. He was placed in a removable body cast to prevent further deformity of the spine.

Fig. 9 (Case 2).—Photograph of patient 18 months after admission, showing residual kyphosis. The patient gained 14 lb. (6,350 gm.) during 21 months of hospitalization.

Initially, streptomycin was begun in a dosage of 1 gm. intramuscularly daily. After one week, this was changed to 1 gm. every second day. After 10 months, the dosage was reduced to 0.5 gm. twice weekly, and this has been continued up to the present time. Paraaminosalicylic acid, 4 gm. daily, was begun with streptomycin and continued for 15 months, at which time it was stopped because of vomiting and anorexia. Isoniazid, 50 mg. orally daily, was begun three months after admission and continued up to the present.

Clinical improvement as evidenced by weight gain and improved disposition became apparent about four months after admission and has progressed steadily. At this writing, 18 months after admission, the patient is an alert active 3-year-old child weighing 31 lb. (14,060 gm.). The only residual of his disease which is apparent on physical examination is the dorsal kyphosis (Fig. 9).

Roentgenograms now show complete healing of the bony lesions, with the exception of those of the 10th and 11th dorsal vertebrae, which are sclerosed and healed with residual angulation.

In spite of his good clinical condition, the chest roentgenogram shows only slight clearing. The trachea is still deviated toward the right. A recent bronchoscopy revealed no bronchial obstruction.

COMMENT

In 1920, Jüngling [1] reported a tuberculous cystic condition of the bone which he termed osteitis tuberculosa multiplex cystica. In 1928, he reviewed 55 cases,[2] the characteristics of which he described as follows:

1. Gradual onset with or without pain in the involved extremity and unaccompanied by fever or general disability.
2. The usual age of onset was 20 to 30 years.
3. Usually the disease involved the small long bones of the hands and feet, rarely the long hollow bones.
4. Skin lesions such as lupus pernio, Boeck's sarcoid, lupus vulgaris, lupus exfoliativus, erythema induratum, and scrofuloderma were associated.
5. The roentgenographic picture consisted of circumscribed areas of rarefaction without periostitis or sequestration.
6. Tuberculin tests and guinea pig inoculations were usually negative.
7. The bone lesions showed no caseation, but were filled with granulation tissue composed of epitheloid cells, fibroblasts, lymphocytes, and occasional giant cells.
8. The cystic areas either remained stationary or healed slowly.

In 1938, Law and Perham [3] reviewed 10 cases in the pediatric literature and reported a similar case of their own in a child. They suggested the following modifications of Jüngling's description of the disease:

1. The disease occurs in children.
2. The long hollow bones may be involved.
3. The presence of cutaneous lesions is not necessary for diagnosis.
4. The tuberculin test may be positive.
5. The primary tuberculous focus is nearly always intrathoracic.

Three additional cases of multiple cystic tuberculosis of the bones in children have been reported by Martin,[4] Martin and Fogel,[5] and Sweet and Abramson,[6] bringing the total to 14 cases. In the majority of these, a primary pulmonary focus was present, tuberculin tests were positive, and bone lesions tended to heal with conservative therapy.

Differential Diagnosis.—In solitary cystic tuberculous lesions of bone, diagnosis may be difficult in the absence of caseation and abscess formation. Benign bone cyst may be suspected, as it was in our first case. Biopsy will disclose tuberculous granulation tissue, but organisms are rarely cultured from the lesion. Pulmonary foci may appear insignificant.

The symptoms and roentgenologic findings in multiple cystic tuberculosis of the bones suggest a number of diagnostic possibilities, such as hyperparathyroidism, multiple myeloma, metastatic malignancy, Boeck's sarcoid, syphilis, pyogenic osteomyelitis, and reticuloendotheliosis. The clinical course and appropriate laboratory procedures will rule out most of these. Biopsy is essential in the diagnosis.

In our first case, the diagnosis was established by guinea-pig inoculation of caseous material. In our second case, histologic evidence of tuberculosis was supplied by bone and lymph-node biopsy. Cultures of the lesions were negative for tubercle bacilli.

Prognosis.—The outcome in cystic tuberculosis of the bones appears to depend upon the extent of tuberculous involvement of the vital organs. Complete healing of cystic areas without residual deformity appears to take place over a period of many months. This occurred in both our patients, the first of whom received no specific therapy. Prognosis must still be guarded in our second case, since there is still extensive pulmonary involvement.

SUMMARY

Two cases of cystic tuberculosis of the bones have been presented. One patient, with a solitary cystic area in the humerus, recovered completely without specific therapy. The second case had multiple cystic lesions involving the skull, vertebrae, and long bones. With streptomycin, paraminosalicylic acid, and isoniazid therapy, his skull and long bone-lesions have healed in a period of one and one-half years, but extensive pulmonary tuberculosis is still present. The clinical picture of our cases conformed to Law's modification of Jüngling's classic description of cystic tuberculous bone disease in early childhood.

Complete healing of cystic areas without residual deformity apparently takes place over a period of many months. The eventual prognosis for life in this syndrome appears to depend upon the extent of tuberculous involvement of the vital organs.

Dr. Robert S. Jason, of the Department of Pathology, was responsible for interpretation of the biopsy specimens.

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PERIARTERITIS NODOSA IN A NINE-MONTH-OLD INFANT

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PERIARTERITIS nodosa in infancy and childhood is relatively rare. About 110 cases up to the age of 15 years have been reported in the world literature. Of these, only 10 cases have occurred during the first year of life.* An additional case of periarteritis nodosa in an infant is presented, in which some unusual clinical, x-ray, and pathological findings appeared. This case had been under observation from the first days of life until death, at the age of 9 months.

REPORT OF A CASE

R. O., a baby girl 6 weeks of age, was admitted to the Department of Pediatrics of the Hadassah University Hospital, Jerusalem, on June 5, 1951, because of vomiting, failure to gain weight, and attacks of fever. These symptoms were said to have been present since birth. At the age of 3 weeks, the patient was admitted to another hospital, at which time cyanosis and crepitant lung rales were found. X-ray examination of the heart and lungs was negative.

The parents were recent immigrants from Yemen and in good health. Two siblings had died of unknown causes during the second year of life. The four remaining siblings were healthy. The infant was normally delivered at term after an uneventful pregnancy.

On admission, the physical examination revealed an undernourished infant weighing 2,960 gm., slightly dehydrated, and moderately cyanotic. Auscultation of the chest revealed coarse rales over both lungs and a harsh systolic murmur over the whole precordium. The ears and throat were normal. The liver was palpable 2 cm. under the right costal margin; the spleen was not palpable.

Laboratory Examinations.—Laboratory findings were as follows: urine, traces of albumin; stool, microscopic examination and culture, negative; RBC, 3,500,000; HGB., 10 gm.; W.B.C., 14,000, with 67% neutrophiles, 3% band forms, 25% lymphocytes, 3% monocytes, 2% eosinophiles; Kahn, negative; cold agglutination, negative; Mantoux 1:1000, negative. No tubercle bacilli were found in the gastric juice. ECG showed right ventricular preponderance. X-ray findings six days after admission, June 11, 1951 (Fig. 1): heart of normal size and shape, hilar markings increased.

Because of the cyanosis and the cardiac murmur, a clinical diagnosis of congenital heart disease was made.

During the first weeks of hospitalization, the patient suffered from acute diarrhea and vomiting, which subsided after administration of sulfadiazine, chlortetracycline (Aureomycin) and a diet of half-skimmed milk. After this occurrence, the infant received an adequate diet, with additional administration of vitamins, ferrous sulfate, and two blood transfusions, but there was no gain in weight. The cyanosis deepened, and the liver enlarged to 5 cm. below the costal margin. The temperature remained normal. Another x-ray of the chest, Dec. 26, 1951 (Fig. 2), revealed slight cardiac enlargement and prominent vascular shadows in the lungs.

From the Departments of Pathology, Pediatrics, and Roentgenology of the Hadassah University Hospital and the Hebrew University-Hadassah Medical School, Jerusalem.

* References 1-9.

After 72 days of hospitalization, the patient was discharged. Her weight was then 2,900 gm., at the age of 4 months.

The child was readmitted to the hospital on Jan. 28, 1952, at the age of 8½ months, in a state of severe marasmus. Her weight was 3,300 gm. Cyanosis and dyspnea were marked. Moist rales were heard over both lungs. During this admission, no heart murmur was detected. The liver and spleen were considerably enlarged.

Laboratory examinations revealed the following: RBC, 3,600,000; HGB, 10 gm., WBC, 10,600, with 56% neutrophiles, 4% band forms, 36% lymphocytes, 4% monocytes, and no eosinophiles. ECG showed right heart strain. X-ray examination on Jan. 28, 1952 (Fig. 3): heart enlarged in all directions; round well-defined shadows scattered in both lung fields, particularly at the right hilum; confluent patchy and hazy shadows in both lung fields. On fluoroscopy, no hilar pulsations were visible.

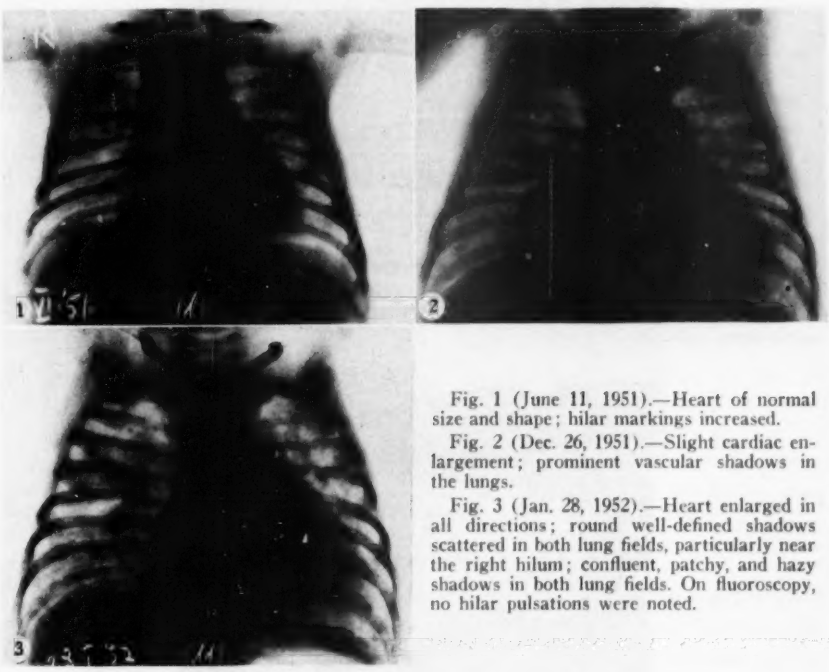

Fig. 1 (June 11, 1951).—Heart of normal size and shape; hilar markings increased.

Fig. 2 (Dec. 26, 1951).—Slight cardiac enlargement; prominent vascular shadows in the lungs.

Fig. 3 (Jan. 28, 1952).—Heart enlarged in all directions; round well-defined shadows scattered in both lung fields, particularly near the right hilum; confluent, patchy, and hazy shadows in both lung fields. On fluoroscopy, no hilar pulsations were noted.

Therapy consisted of penicillin, chlortetracycline, and the administration of oxygen. The patient's condition deteriorated progressively until her death, on the 10th day of the second hospitalization.

Autopsy Findings.—The body was that of a marantic baby girl, 56 cm. in length, weighing 2,800 gm. The skin was inelastic and brownish-gray in color and lacked subcutaneous fat. The chest was flattened, the abdomen protuberant. The skeletal muscles were atrophic.

Lungs.—The most obvious changes were in the medium-sized and small arteries. The walls of almost all arteries were thickened up to 2.5 mm. in width, and the lumina were markedly narrowed. Here and there the vessels were converted into oval-shaped nodules of dense fibrous tissue in which the lumina were invisible (Fig. 4). There were foci of emphysema, hemorrhages, and hemorrhagic infarctions scattered throughout both lungs. The bronchial tree was not involved.

Heart.—The heart weighed 50 gm., and all chambers were enlarged. The coronary arteries were diffusely thickened up to 3 mm. in diameter. On cross section, fibrous thickening of the

walls and extreme narrowing of the lumina was apparent. The right ventricle was slightly larger than the left; the wall of the right ventricle was 5 to 6 mm. thick in the region of the pulmonary conus. The endocardium and the leaflets were thin and smooth.

No macroscopic changes were found in the other organs.

Microscopic Examination.—Lungs: The most prominent changes were in the pulmonary arteries of the muscular type. The intima was markedly thickened by fibrosis and the lumina correspondingly narrowed or completely occluded (Fig. 5). Within all layers of the arterial walls

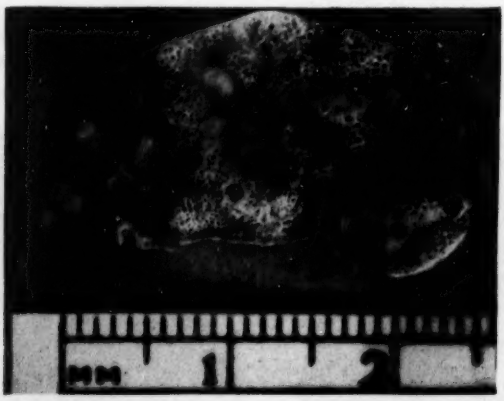

Fig. 4.—Cut section of the lung. Pulmonary arteries are markedly thickened or converted into oval-shaped fibrous nodules. Hemorrhagic infarctions, left side of section; emphysema and hemorrhages, right side.

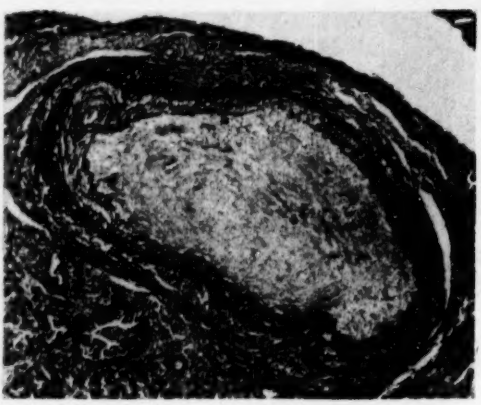

Fig. 5.—Pulmonary artery enlarged and completely obliterated by dense fibrous tissue. Elastic tissue destroyed in some places (Verhoeff's stain, × 155).

were scattered foci of neutrophiles, lymphocytes, and plasma cells, most often in the intima. Several vessels were occluded by recent, or partially, or completely organized thrombi. Verhoeff's stain for elastic tissue showed disruption of the internal elastic lamina and the elastic fibers of the media in some arteries.

Fibrinoid necrosis was seen in a few of the scarred vessels in the form of fine bands located in the intima, generally next to the lumen (Fig. 6) or near the media. Segmental necrosis of the entire wall was observed only in vessels 100 to 150 μ in diameter. Giant cells and granulomas were not seen.

The above-mentioned changes were also present in several bronchial arteries. Other findings in the lungs consisted of emphysema, small hemorrhages, atelectasis, bronchopneumonia, and edema, all focal in nature.

Heart: Changes similar to those described in the pulmonary arteries were seen in the large coronary arteries and their branches located in the epicardial fat. The intramural branches of the coronary arteries were not affected.

Kidneys: Only the large interlobar arteries situated in the peripelvic fat tissue and some of their branches showed lesions similar to those found in the lungs and heart.

Other Organs: A few arteries 150 to 500 μ in diameter, located at the root of the mesentery, in the portal spaces of the liver, and in the peripancreatic and periadrenal fat (Fig. 7) were involved by acute, healing, and healed lesions.

Final Pathologic Diagnosis.—The final pathologic diagnosis was periarteritis nodosa in the healed and healing stage, involving the pulmonary, bronchial, coronary, renal, and mesenteric arteries, with a few acute lesions of mesenteric, pancreatic, adrenal, and hepatic arteries.

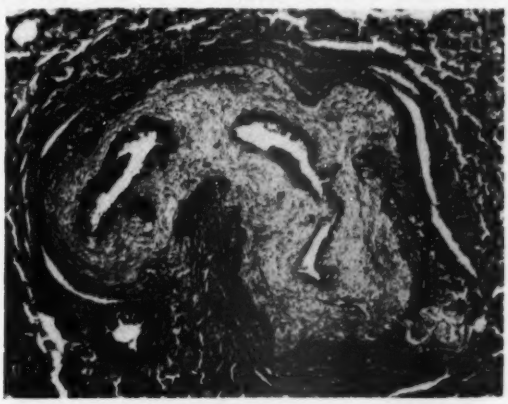

Fig. 6.—Pulmonary artery with typical changes of periarteritis nodosa in the healing stage. Recent fibrinoid necrosis in the thickened intima near the lumen (Verhoeff's stain, × 155).

COMMENT

The diagnosis of periarteritis nodosa during life is difficult because of the great variety of the clinical manifestations of the disease. Of the 10 cases of periarteritis nodosa reported in infants under the age of one year, only one was diagnosed during life, by histological examination of a subcutaneous nodule.[5] Most of these cases in early infancy were characterized by short duration. Usually an initial infection was followed by urticarial or purpura-like rashes, and sudden death occurred before any definitive clinical diagnosis was made. In the case described by Thinnes,[2] death was preceded by sudden abdominal pain of only four hours' duration.

In the present case the course was protracted and initiated by fever and gastrointestinal disturbances. The findings of cyanosis, arrested development, heart murmur, enlarged heart, and signs of progressive cardiac failure seemed to justify the clinical diagnosis of congenital heart disease of the cyanotic type.

The x-ray findings of increased vascular markings in the lung fields and of a heart which increased in size over a short period of time favored the diagnosis of one of the varieties of transposition of the great vessels. However, this diagnosis was

doubted because the aortic shadow was not narrowed in the anteroposterior position and was not widened in the left antero-oblique. The possibility that the pulmonary changes were secondary to chronic cardiac failure was excluded during the last weeks of life, when x-rays showed well-defined vessels and no areas of pulmonary edema or pleural involvement. An inflammatory lesion such as bronchopneumonia does not usually produce the round well-circumscribed hilar shadows found in this case.

The remaining clinical findings, such as the slight anemia, the leucocytosis, and the traces of albumin in the urine, although usually found in periarteritis nodosa, were too nonspecific in nature to be of any help in diagnosis. Eosinophilia in the peripheral blood, which sometimes is suggestive of periarteritis nodosa, was absent in this case.

The most interesting feature of the autopsy was the signs of healing of the disease. Most of the vascular lesions were old, fibrotic, and acellular. Even the acute lesions,

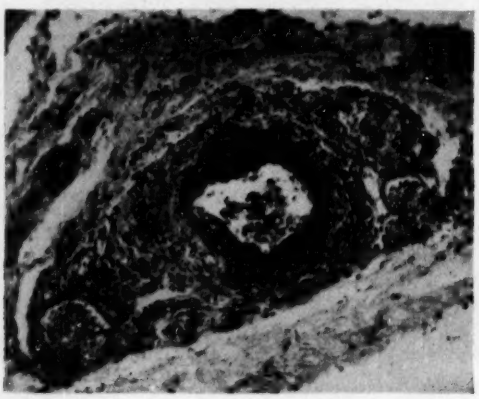

Fig. 7.—Small artery in the periadrenal fat, revealing an acute lesion with only slight inflammatory reaction (hematoxylin and eosin, × 160).

which were few and found only in small arteries, showed but a slight degree of edema, fibrinous exudation, and cellular infiltration devoid of eosinophiles.

The fibrinoid necrosis present in the intima of the thickened pulmonary arteries (Fig. 6) may be considered as a sign of a recurrent wave of the disease. However, it also may be a result of increased vascular tension in the pulmonary system, developing from the thickening of the arteries and reduction of their lumina.

The pulmonary and bronchial arteries in adults are affected by periarteritis nodosa in about 12 to 28% of the reported cases.† In children up to the age of 15 years, the lungs are only occasionally involved. The present case is the only one in which periarteritis nodosa has been found in the arteries of the lungs in an infant during the first year of life.

The coronary arteries, however, are more frequently involved in children. Among the 10 cases of periarteritis nodosa reported in infants below the age of one year, only 1 presented clinical symptoms compatible with congenital heart disease.[8] In

† References 10-12.

all the other cases cardiac signs were not prominent clinically, but at autopsy in all these cases the coronary arteries were found to be involved, in three cases even by multiple aneurysms.‡ Sinclair and Nitsch's patient [7] died from pericardial hemorrhage originating in a ruptured aneurysm.

Concerning the pathogenesis of the disease, nothing new can be added to the present knowledge. Wilmer,[6] reporting two cases occurring in babies 10 and 25 days of age, felt that the disease developed during the fetal period of life. It was assumed that this might have occurred also in the present case, in view of the clinical manifestations appearing shortly after birth.

SUMMARY

The clinical, x-ray, and pathological findings in a case of periarteritis nodosa occurring in a 9-month-old infant are described. The lesions were in the healed and healing stage of the disease and confined predominantly to the lungs and heart.

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CHYLOUS MESENTERIC CYST CAUSING VOLVULUS OF MALROTATED INTESTINE

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APPROXIMATELY 500 cases of mesenteric cysts of all types had been reported in the literature up to 1935, and it is conjectured that between 200 and 300 were of the chylous variety.* In 1947, Beahrs and Judd reported an incidence of 7 chylous cysts in over 1,000,000 patients at the Mayo Clinic.[3] Block estimates that 1 case of chylous mesenteric cyst occurs in 150,000 admissions in general hospitals.[4]

Chylous cysts vary in size, are usually single, and lie between the peritoneal leaves of the mesentery of the small bowel, usually the jejunum. Since they are not tensely filled, they tend to be flabby. A dumbbell shape is common, with the cyst projecting out from either side of the mesentery, partially surrounding a loop of bowel, like a saddle. The walls are thin, consisting of connective tissue and an inner lining of endothelial cells. Gross emphasizes the absence of a muscle coat as a feature distinguishing the chylous from the enterogenous variety.[5] However, Thompson and Chambers state that chylous mesenteric cysts may have bundles of smooth muscle in the walls.[6]

Mesenteric cysts must be differentiated from enteric cysts, which are actually duplications. Four features serve as points for comparison. Mesenteric cysts have thin walls, with no true muscle coat or mucosa, and, although they may lie against the intestine, there is a line of cleavage between the two which permits excision without injury to the bowel or its blood supply. Enteric cysts, on the other hand, have thick walls containing all layers of intestine, lie adjacent to the bowel, have a musculature so intimately associated with that of intestine that they cannot be separated without injury to the latter, and, finally, have a vascular supply in common with the adjacent intestine, so that excision of the cyst compromises the blood supply, necessitating bowel resection.

Various theories have been proposed to explain the origin of chylous cysts.

I. Obstruction of a lymphatic trunk. This theory is questioned on the ground that a cause of obstruction is never found, e. g., inflammation with fibrosis. Moreover, cyst formation from obstruction of a single lymphatic trunk is not likely because of the rich anastomosis of lymph vessels in the mesentery and retroperitoneal region.

II. Preexisting cysts. Dowd, Warfield, Higgins, and Lloyd regard chylous cysts as accumulations of chyle in preexisting cysts.†

III. Embryonic rests. Brindley feels that chylous cysts may arise from embryonic rests of lymphatic tissue and that they are really lymphangiomas, inasmuch as

Dr. Joseph Catanese assisted in the medical management of this case.

* References 1 and 2.

† References 7, 2, and 8.

they are endothelium-lined neoplasms containing lymph.[9] In fact, Beahrs calls them "chylangiomas."[3]

The most likely etiology is that these cysts develop from misplaced islands of lymphatic tissue which proliferate and accumulate chyle because they do not communicate with the remainder of the lymphatic system (Gross).[5]

Chylous cysts are rarely detected in infancy, and the diagnosis is seldom made preoperatively. The patient may complain of a slowly enlarging abdomen. There may be recurrent attacks of abdominal pain, at times associated with vomiting. In the cases reported, the presenting symptoms have usually been those of an acute surgical complication, such as intestinal obstruction resulting from volvulus; angulation of bowel; adhesions or intussusception; rupture, torsion, or incarceration of a cyst; pressure on organs, notably the intestines, and peritonitis resulting from hemorrhage.‡

One of the rarer complications of a mesenteric cyst is intestinal obstruction due to volvulus. The volvulus is more likely to occur if there is malrotation of the bowel from twisting around the mesenteric axis; the short mesenteric attachment in these cases favors involvement of the entire small intestine.

The treatment of chylous mesenteric cysts is surgical. Simple enucleation has the lowest mortality rate (9%). When resection of the intestine is necessary, the mortality increases to 25 to 30%.[1] Marsupialization carries with it a mortality of 16%,[1] plus the complications of persistent sinus, nonobliteration, and, quite frequently, intestinal obstruction.[3] When complicated by intestinal obstruction due to volvulus, the mortality rate is extremely high. Gross reports excision of five chylous cysts. Two were associated with volvulus; both patients died. It is with particular interest, therefore, that we present a case of chylous mesenteric cyst causing volvulus of malrotated intestine, with survival following surgery.

REPORT OF A CASE

W. B., a 6-year-old white boy, was admitted to the Albert Einstein Medical Center, Aug. 4, 1951, complaining of generalized abdominal pain and vomiting of 16 hours' duration. For several years there had been progressive enlargement of the abdomen, recurrent attacks of pain and vomiting, and poor appetite. Examination of the abdomen revealed moderate distention, dullness, and vague tenderness. Urinalysis was negative. Hemoglobin was 95% and the leucocyte count 12,000, with 87% polymorphonuclears. Operation was performed shortly after admission.

On exploration, a pinkish thin-walled cyst was found, almost completely occupying the abdominal cavity. The entire small bowel was purple, with marked edema and petechial hemorrhages in the mesentery. Because it was impossible to deliver it intact, the cyst was opened and more than 1,500 cc. of milky fluid was drained. After collapse, it became apparent that the cyst was located between the leaves of the mesentery of the distal jejunum (Fig. 1). The cyst was excised, with preservation of blood supply to the small bowel. In the mesentery of the jejunum, there were several smaller cysts, likewise filled with milky fluid; these were enucleated.

Further observation revealed that the mesenteric attachment of the entire small bowel was no more than 1½ in. (3.8 cm.) in length and was located just below the ligament of Treitz; the small bowel was twisted on its mesentery. The volvulus had apparently been created by movement of the cyst, which caused torsion around the short mesenteric attachment. When the mesentery was untwisted, the small intestine immediately resumed its normal color.

Continued exploration revealed that the cecum was located in the right upper quadrant of the abdomen. The appendix lay retrocecally, extended up under the liver, and was covered completely by a peritoneal fold; it was mobilized and removed.

‡ References 10 and 11.

The pathologist described the cyst as having a thin smooth gray wall, with slight trabeculations on its inner surface. Sections of the wall revealed fibrofatty tissue and smooth muscle bundles, with a few lymphocytes; no lining membrane was discernible (Fig. 2). There was

Fig. 1.—Photograph taken during the operation. The partially emptied cyst is lying in a basin beside the abdomen. The cyst originates in the mesentery of the distal jejunum.

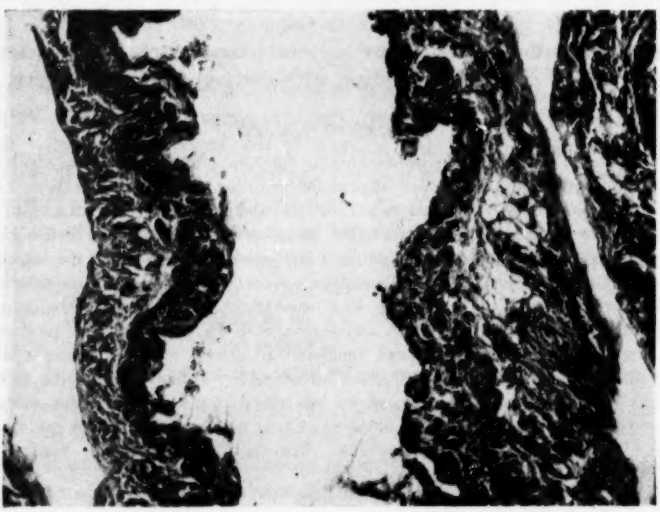

Fig. 2.—Photomicrograph of cyst wall. Note fibrofatty tissue, smooth muscle bundles, and absence of lining membrane; × 15.

no evidence of malignancy. It is interesting to note that the appendix showed mild inflammation, due to Enterobius vermicularis infestation.

The patient was discharged on the ninth postoperative day, following an uneventful convalescence. At the time of this writing, two and one-half years from the time of surgery, the patient enjoys good health and shows no evidence of recurrence.

COMMENT

The case reported presents several interesting features. In the first place, the cyst, containing 1,500 cc. of fluid, is apparently one of the largest on record; the largest of all mesenteric cysts reported by Gross contained 1,200 cc.[5]

The presence of smaller cysts lends support to the contention that chylous cysts arise from misplaced pieces of lymphatic tissue.

The malrotation was of the type in which the cecum remains in the region of the gall bladder. The conjecture is warranted that perhaps the cyst may have already been forming in utero and was actually the cause of the malrotation. In any case, one may postulate that the twisting of the cyst initiated the volvulus.

The matter of diagnosis is worthy of comment. In this instance, the condition was not suspected until the time of operation. The patient had been seen by several physicians over several years because of progressive abdominal enlargement, associated with pain and vomiting. One must emphasize, therefore, the importance of suspecting mesenteric cysts in the presence of slowly progressive abdominal enlargement, especially in children.

The case under discussion was treated by excision, the method of preference. Consideration of pathology, therefore, must always be taken into account, inasmuch as enterogenous cysts require resection of the involved intestine.

SUMMARY

A rare case of chylous mesenteric cyst is reported. As far as can be determined, the cyst is the largest on record. Moreover, it presented the unusual complication of volvulus of a congenitally malrotated small bowel.

Chylous mesenteric cysts are considered from the standpoint of incidence, etiology, pathology, diagnosis, and treatment, together with a review of the literature.

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FERROUS SULFATE POISONING

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TOXIC effects from the ingestion of large doses of medicinal iron preparations have received increasing attention since 1947, when Forbes [1] reported two fatal cases. Since his report, 24 additional cases have appeared in the medical literature.* In all, 25 infants and 1 adult were involved. Ferrous sulfate was ingested in 25 cases and ferric chloride in 1 case. Thirteen cases were fatal, and in 13 there was recovery. There seems to have been no direct correlation between the amount of iron ingested and the final outcome, since the ingestion of as little as 3.0 gm. of ferrous sulfate has terminated fatally,[8] whereas the ingestion of 15.0 gm. has resulted in an uneventful recovery.[11]

Case 1 of the present study recovered after the ingestion of 2.4 gm. of ferrous sulfate. In Case 2, the ingestion of 10.2 to 14.2 gm. of ferrous sulfate proved fatal. The typical biphasic clinical course and the histopathologic findings are emphasized in the light of previous reports. The rationale of possible surgery in the future management of such cases is discussed.

REPORT OF CASES

CASE 1.—S. M., a 15-month-old white baby girl, was admitted to the Chanute Air Force Base Hospital on Dec. 12, 1952, with a history of having ingested eight 0.3-gm. enteric-coated ferrous sulfate tablets 17 hours previously. Two hours after ingestion of the tablets, she vomited partially digested food, but no blood or tablets were noted. The examination was negative at this time, except for listlessness. She was sent home on a milk diet, but the parents were advised to return if hematemesis or melena developed. That night the child slept fretfully and was irritable and feverish. Upon awakening in the morning, she passed a large pitch-black formed stool.

The physical examination upon admission revealed a temperature of 104 F., a mild and apparently subsiding right catarrhal otitis media, and marked irritability. The urinalysis was normal. The white blood cell count was 48,000, with 55% neutrophiles, 41% lymphocytes, 2% monocytes, and 2% eosinophiles. The hemoglobin was 11.0 gm. and the red blood cell count 3,500,000. The child was placed on a regimen of 300,000 units of aqueous penicillin procaine daily and given 15 cc. of liquid petrolatum (mineral oil) per os. A tap-water enema returned a small amount of formed grayish-colored stool. Her temperature returned to normal

From the Department of Pediatrics and the Laboratory Service, Chanute Air Force Base Hospital, Rantoul, Ill.

* References 2-14.

in about 24 hours, and the child ate and drank well. On the subsequent days of hospitalization she was afebrile, was not unduly irritable, had normal stools, and did not vomit. The otitis media gradually cleared. On the second hospital day, the white blood cell count was 54,900, with 87% neutrophiles. On the third day, it was 5,650, with a normal differential count. She was discharged the following day with a normal blood cell count and has since remained well.

Case 2.—A. L., a 20-month-old white girl, was admitted to the Chanute Air Force Base Hospital on March 17, 1953. She had been found playing with an empty pillbox four hours previously, and it was assumed that she had ingested from 34 to 44 0.3-gm. enteric-coated ferrous sulfate tablets. One hour after the ingestion, she vomited a yellow-green fluid with some partially digested food. No tablets were noted in the vomitus. Three hours after the ingestion, the vomiting had become almost continuous and was definitely bloody. Diarrhea supervened. The stools were greenish-black and liquid but contained no gross blood. Marked pallor developed, and the skin became cold and clammy. The child was brought to the hospital four hours after ingestion of the tablets.

Physical examination upon admission revealed an acutely ill infant who was vomiting blood-tinged fluid and had a bloody diarrhea. She was pale and mildly cyanotic and responded only to the strongest of stimuli. Her temperature was 101 F., blood pressure 70/0, and pulse rate 160. The abdomen was mildly distended. The remainder of the physical examination was negative. The white blood cell count was 12,100, the red cell count 4,100,000, the hemoglobin 12.0 gm., and the carbon dioxide combining power 27.5 vol. %.

She was placed in oxygen and given 150 cc. of 5% dextrose in isotonic saline, 250 cc. of 5% dextrose in water, 250 cc. of whole blood, and 250 cc. of 1/6 M sodium lactate intravenously; 300,000 units of aqueous penicillin procaine and 5 mg. of vitamin K were given intramuscularly. During and after the intravenous fluid therapy, the child became alert, responded to her parents, and asked for water (which was denied). The vomiting subsided, and there was a decrease in the bloody diarrhea. Her color improved, and the blood pressure rose to 120/70. Her temperature was 103 F. For the next six hours the child had less diarrhea, no vomiting, and a normal blood pressure. The red blood cell count was now 5,130,000, the hemoglobin, 13.5 gm., and the white cell count, 24,900, with 52% neutrophiles, 47% lymphocytes, and 1% eosinophiles.

About nine hours after admission, the child began to vomit again and developed an almost continuous bloody diarrhea. The vomitus contained clotted and liquid blood. At this time she was fed several strips of absorbable gelatin sponge U. S. P. (Gelfoam) moistened in isotonic saline. No change in the vomiting was seen. Another 250 cc. of whole blood was given intravenously. Although severe vomiting and diarrhea continued, the red blood cell count and the hemoglobin remained at 4,880,000 and 13.5 gm., respectively. Gradually, the blood pressure dropped until it was unobtainable and the pulse rose to 200. The child became cyanotic while in oxygen and deeply comatose and had repeated convulsions. Cheyne-Stokes respiration developed about 12 hours after admission, and she died 16 hours and 40 minutes after admission, or 20 hours and 40 minutes after ingestion of the tablets.

At postmortem examination, performed five hours after death, the body weighed 11,000 gm. and measured 83 cm. The pertinent gross and microscopic findings were as follows: A sharply localized segment of infarcted ileum was immediately evident upon opening the abdomen. The peritoneal fluid was scant. The blood in the larger vessels was fluid and without coagula.

The heart weighed 75 gm. The right auricle and ventricle were markedly dilated, and the pulmonary conus was moderately dilated. The right lung weighed 145 gm., the left lung 130 gm. Both lungs were boggy to palpation. The smooth mottled dusky-red surfaces revealed multiple 0.4-cm. areas of subpleural hemorrhage. On section, the dark red surfaces oozed considerable amounts of frothy reddish-white thin fluid. The mucosa of the left main-stem bronchus appeared dull and edematous, with small masses of brown semisolid material stuck to it. The liver weighed 440 gm. About the entrance of the portal vein and extending thence to involve roughly 30% of the liver the cut surface assumed a mottled brownish-grey color, appearing partially necrotic. In other areas the liver was grossly normal.

The esophagus was normal. The stomach contained about 10 cc. of a reddish-gray granular fluid material; however, the mucosa was well preserved. The duodenum and jejunum appeared normal. The entire small bowel measured 200 cm. in length. Eighty centimeters from its proximal

end, small areas of erosion and enlarged ulcerated Peyer's patches first appeared. This condition grew more pronounced for the next 20 cm., at which point the entire bowel wall abruptly assumed a purplish infarcted appearance. The strip of infarcted ileum was 15 cm. in length. The lumen was distended by reddish-purple granular necrotic semifluid material. The mucosa was entirely sloughed. Large ulcerated Peyer's patches were prominent (Fig. 1). The serosa

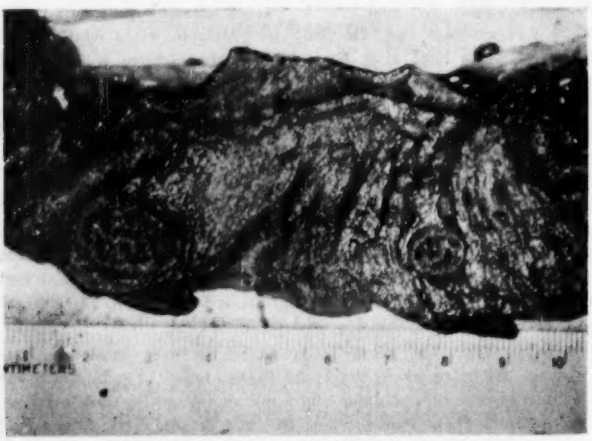

Fig. 1.—A segment of infarcted ileum, showing sloughed mucosa and two hyperplastic Peyer's patches with central ulceration.

Fig. 2.—A section of ileum from Figure 1, showing complete mucosal erosion, hyperplasia, and ulceration of Peyer's patch. The dark discoloration of the intestinal villi (iron pigment) is evident; × 440.

was dull and purple. The bowel mesentery at this point revealed dilated thrombosed venous channels. Eight to 10 large (up to 1.5 cm.) firm hemorrhagic lymph nodes were found adjacent to the region of infarcted ileum. The remainder of the small bowel showed similar but steadily diminishing mucosal changes and was viable. The large bowel was normal.

Microscopic examination of the most severely involved portion of ileum revealed an edematous infarcted bowel wall, with massive hemorrhage throughout the submucosa. The epithelium of the

villi and gland lumina was completely sloughed. The necrotic villi showed a marked brown granular discoloration, especially at their tips (Figs. 2 and 3). The submucosal vessels and the vessels of the lamina propria were dilated and contained masses of dark brown granular pigment. The pigment was most prominently distributed at the vessel periphery (Fig. 3). The Turnbull blue stain for ferrous iron was positive for this pigment and for that involving the

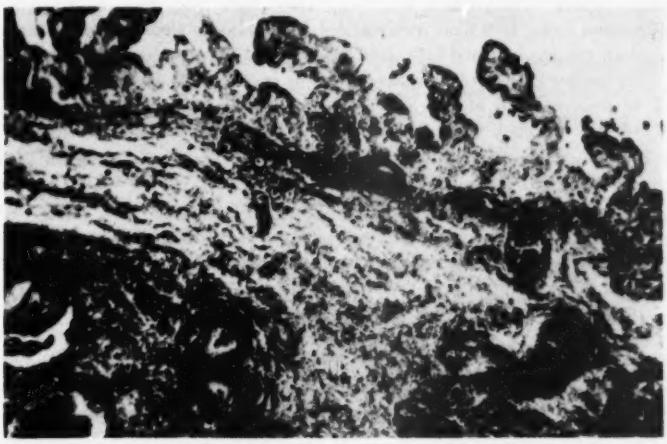

Fig. 3.—The ileum, showing thrombosed venous channels, with granular pigment material distributed at the vessel periphery. The pigment is iron-positive × 100.

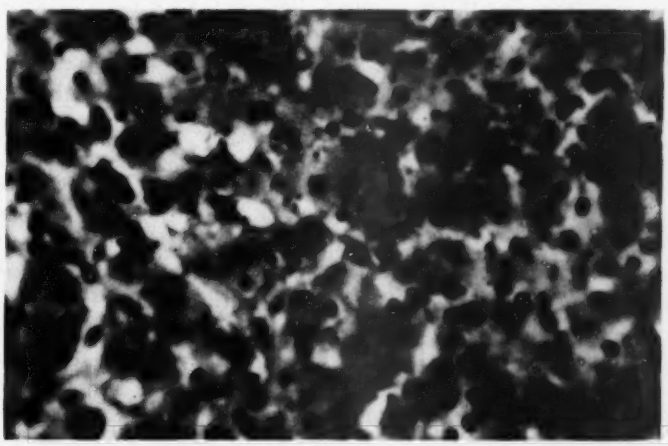

Fig. 4.—The liver, showing early necrotic changes manifested by cloudy swelling and dissolution of hepatic nuclei; × 440.

villi. There was profound hyperplasia, edema, and architectural distortion of the focal lymphoid follicles in the submucosa, with ulceration of overlying mucosa (Fig. 2).

In areas less severely involved, the edematous ileum showed sloughing of the epithelium over the villus tips; however, the epithelium at the bottom of the glands was preserved. Hyperplasia of Peyer's patches was also noted, but with less edema and no architectural distortion. The esophagus, stomach, and large bowel were normal.

The lymph nodes draining the infarcted segment were hyperplastic and hemorrhagic, with large distinct germinal centers. The wide, edematous, bloody lymphatic channels were jammed with neutrophiles, lymphocytes, and large mononuclear cells. No iron pigment could be demonstrated.

In the lungs, an extensive intra-alveolar hemorrhagic extravasation was noted. The alveolar walls were profoundly hyperemic. The bronchial epithelium was focally eroded and the small vessels greatly dilated. The peribronchial lymph nodes were hyperplastic and focally engorged with blood, round cells, and some neutrophiles. The hepatic sinusoids were engorged with blood. In areas, the parenchymal cells showed marked cloudy swelling, with focal dissolution of nuclei. The nuclear changes were characterized by marked peripheral clumping of chromatin, proceeding to disappearance of the nuclear membrane and scattering of chromatin material within the cell. The Turnbull blue reaction was negative in both lung and liver.

Permission to examine the brain was not granted. Other organs, including the kidneys, were normal grossly and microscopically.

A chemical analysis of the liver revealed 0.2 mg. of inorganic iron per gram. This is actually a low value. The gastric contents contained 1.2 mg. of inorganic iron per milliliter and the intestinal contents 1.1 mg. of inorganic iron per milliliter.

COMMENT

There is a fairly characteristic set of symptoms of iron poisoning. The clinical picture of Case 2 is similar to many of the reported cases. Within an hour of ingestion of the tablets, vomiting develops, which in two to four hours usually becomes bloody. The child becomes pale, irritable, and often comatose; the blood pressure falls, the pulse becomes rapid, and the child appears in profound shock. Diarrhea may or may not be present at this stage. Half of the reported fatalities were during this stage. Following this period of shock, there is often a rapid improvement in the clinical picture, during which the patient regains consciousness and is out of shock, and the vomiting and diarrhea decrease. However, in many cases there will occur a sudden relapse from 13 to 40 hours after ingestion, in which the child again goes into profound shock, with coma, severe bloody vomiting and diarrhea, and, frequently, convulsions.

The necropsy findings are also fairly characteristic. In all but one of the autopsied cases there was marked dilatation of the right heart, with pulmonary congestion and hemorrhage. Cloudy swelling or early necrosis of the liver were frequently observed. In general, a hemorrhagic necrotizing gastritis followed the ingestion of plain coated tablets, whereas a similar localized enteritis resulted from the ingestion of enteric-coated tablets, due to their liberation in the lower gastrointestinal tract. Three of the fatal cases involved enteric-coated tablets; one of these was associated with necrosis of the gastric mucosa, and the other two with necrosis of the small intestine. Plain tablets were ingested in the remaining 10 fatal cases, and all of these showed necrosis or marked congestion of the gastric mucosa. Two of these also showed necrosis of the small intestine, one having ingested approximately 20 gm. of ferrous sulfate and the other 240 gm. In our second case, it would appear that the enteric-coated tablets proceeded down the intestinal tract relatively intact until the enteric coating was finally dissolved at the isolated segment of necrotic ileum.

Case 1 is interesting because of the high white blood cell count, of 54,900, which persisted for about 60 hours. In Case 2, the white cell count reached 24,900. Marked

leucocytosis has also been reported in some of the other cases: 37,800, in the case of Swift and co-workers,[13] 21,750, in one of Duffy and Diehl's cases,[12] 79,000, in Lindquist's case,[7] and 55,750, in Foucar's case.[9] The significance of these elevations is unknown.

The treatment of iron poisoning is largely symptomatic. Immediate efforts should be made to make the child vomit in order to rid the stomach of any undissolved tablets or fragments of tablets. In addition, copious and prolonged gastric lavage should be done with sodium bicarbonate solution, leaving some in the stomach in an effort to convert the ferrous sulfate to insoluble ferrous carbonate. Shock should be combated with blood, plasma, and oxygen as indicated, and one should be alert for the possibility of a delayed exacerbation after initial improvement. Roxburgh [5] used dimercaprol (BAL) in the treatment of a 16-month-old patient who recovered from iron poisoning, but he made no claim for benefit from it. Animal experimentation indicates that the toxic effects of ferrous sulfate are aggravated by dimercaprol.[6] Spencer [8] has suggested use of the following prescription in cases of iron poisoning:

Thiamine hydrochloride	10 mg.
Nicotinamide	30 mg.
Riboflavin	10 mg.
Tocopherol	15 mg.
Methionine	500 mg.

Multiply the above amounts by the patient's age in years and give in three divided doses daily.

It is suggested that the iron, acting as a heavy metal, may combine with —SH groupings and thus interfere with oxidation. The tocopherol is given in an effort to reduce the oxidative requirements of the cells and the methionine as a source of —SH groupings and as protection for the liver.

It is well known to radiologists that enteric-coated iron tablets are radiopaque. If an x-ray of the abdomen reveals iron tablets grouped together in the intestine, a localized patch of gangrene of the intestine such as was found in our second case is to be expected. If so, a laparotomy should be considered after recovery from the initial shock stage to remove the tablets and to resect the necrotic segment of bowel.

SUMMARY

Two cases of iron poisoning are presented. The clinical features and pathology of the condition are reviewed and the available forms of treatment discussed. The use of surgery in selected cases is suggested.

The photographs of Case 2 were taken by Technical Sergeant Roland J. Englehardt. University of Oregon Medical School, Portland, Ore. (Dr. Clark).

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OSTEITIS PUBIS

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OSTEITIS pubis is a very rare clinical entity in the pediatric age group. Although there are many reports of this disease in the literature, they are confined to adults and occur after operative procedures upon the genitourinary system, usually prostatectomies. The disease is characterized by a self-limiting nonsuppurative osteonecrosis of the pubic bones, usually beginning at the symphysis pubis and extending along the pubic rami in a rather symmetrical fashion, and may extend so as to include the ischial tuberosities. Although the bone destruction may be extensive during the active course of the illness, recovery occurs with complete regeneration of the pubic bones, and often ankylosis of the symphysis results.

The disease was first described in 1924, by Beer, who noted this as a peculiar complication following a simple suprapubic prostatectomy. Since that time, there have been numerous reports of cases occurring several weeks to several months after suprapubic prostatectomies, retropubic prostatectomies, and bladder operations. Interested in this rather rare entity, Beer compiled case reports and in 1928 published a summary of the clinical syndrome following suprapubic prostatectomies.[2] He believed that the etiology, although obscure, was related to infection developing in the periosteum as a result of injury sustained in this type of procedure. Beach [1] reported seven cases, all following genitourinary operations, and stated that the cause was probably directly related to the collection of the spilled urine, inherent in these procedures, behind the pubic bodies; he postulated that the condition would be restricted to the male, owing to the anatomic arrangement of the pelvic fascia. Mortensen [9] reported 44 cases following genitourinary surgery. Other similar reports have occurred relatively frequently in the urological literature. Lavalle and Hamm [6] stated that it is a true inflammatory disease of the anterior pelvic girdle and not a sterile necrosis of bone as found in Sudeck's atrophy. Klinefelter [5] has described a case occurring in a 16-year-old boy who sustained an injury over the symphysis and right pubic ramus while playing basketball, with the onset of symptoms 21 days later. Vest [6] has mentioned two mild cases found in football players. Kleinberg [4] reported a case occurring in a female following pyelonephritis. Wilensky [12] described a similar entity following symphysiotomy in a female and again in a patient with a vaginal fistula to the pubic bone. McGinn [8] wrote of osteitis pubis following ureterolithotomy.

At any time from a few days to several months after trauma, there is an abrupt onset of severe pain in the midline over the pubic bones, often excruciating in

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nature, and the area is exquisitely tender to palpation. Occasionally the onset may be relatively benign, with vague pain in the back and in the groin. Pressure over the symphysis elicits pain, usually to the side of the midline. Extension along the pubic rami manifests itself by pain in the inguinal regions and in the region of the thighs, especially along the medial aspects. There is a spasm of the muscles that have their attachments to the affected bones. This concerns primarily the adductor group of the thigh as well as the levator group. The rectus muscles are tense, and there is pain on coughing or on attempts to sit up. Any movement of the pelvis induces severe pain, since this causes contraction of the muscles, and the patient is in morbid fear of being moved. The legs can be crossed only with great difficulty and cannot be widely abducted. The patient cannot stand or sit comfortably, generally lies with the thighs flexed on the abdomen, and may have difficulty in changing body position. An abnormal gait, simulating congenital dislocation of the hip, may be found. Pain may radiate to the perineal area, causing contraction of the levator muscle group and precipitating painful micturition and defecation.

The x-ray findings may be grouped into three phases—prodromal, destructive, and regenerative. The first roentgenograms show no abnormalities or, perhaps a slight fraying at the margins of the symphysis. Within a week the destructive phase appears. There is progressive decalcification of the pubic rami beginning at the symphysis, which imparts a moth-eaten appearance to the bones and represents acute bone atrophy. Eventually there is a symmetrical U-shaped area of loss of bone and cartilage at the symphysis and fraying of the periosteum in the region of the muscular attachments. This osteolytic activity is observed for four to six weeks, and gradually healing ensues, accomplished by recalcification at the margins of the lesion, reducing the defect in a rather orderly fashion. After several months there is complete bony restitution, and bony ankylosis ensues in the symphyseal region. No sequestration is seen, and no suppuration has been reported, although Friedenberg described a case in which suppurative arthritis of the hip developed after an episode of osteitis pubis, with ultimate destruction of the hip joint.

Laboratory studies are of little value in this syndrome. The white blood cell count is only slightly elevated, if at all. There may be mild secondary anemia.

REPORT OF A CASE

A 6½-year-old Negro boy was admited to Saint Luke's Hospital, July 17, 1952, with a chief complaint of difficulty in voiding and pain around the rectum of two days' duration. Sudden onset of pain in the lower abdomen and in the pelvic region occurred three days prior to admission, and the child felt "feverish," although his temperature had not been taken. Voiding became a difficult task, taking 10 to 15 minutes to accomplish, and was associated with much discomfort. For the preceding two days, enemas were necessary to effect a bowel movement. He was not able to walk or to sit comfortably and bitterly complained of pain in the lower abdomen and in the pelvic region. The child had recently had varicella and had fully recovered a week prior to the onset of symptoms. There was also a vague history of a fall about 10 days previously. Other past history and family history were noncontributory.

Physical examination on admission revealed a well-developed, well-nourished Negro boy, not appearing acutely or chronically ill, quiet and comfortable when not disturbed. He assumed a partially flexed position on the examining table and complained of severe pain when his hips or legs were manipulated or straightened. The left thigh was flexed on the abdomen and was particularly resistant to motion. When the left leg was moved, pain and adductor spasm were

encountered. Abdominal examination revealed no spasm or rigidity. There were pain and tenderness in both inguinal regions, but the maximum point of pain was over the suprapubic area in the midline, extending slightly to the right. No lymphadenopathy was present. Rectal examination was negative, except that it confirmed the tenderness anteriorly and to the right. On palpation, the prostate gland was not found to be enlarged. The temperature was 100 F., the

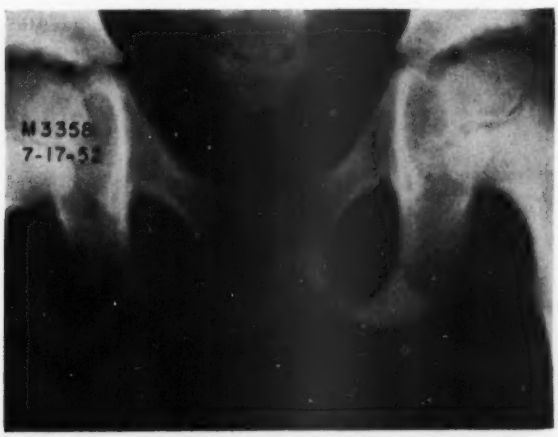

Fig. 1.—X-ray of the pubic symphysis (normal) upon admission.

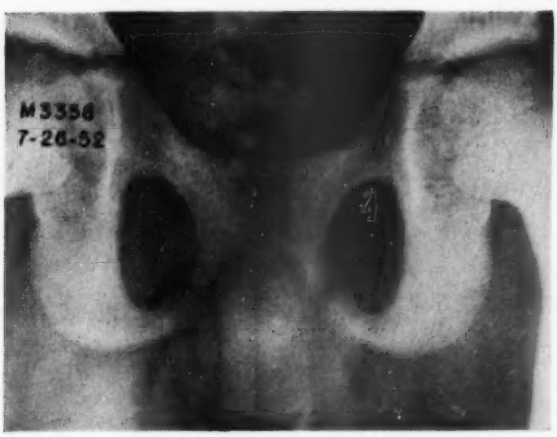

Fig. 2.—Bilateral destruction at the bodies of the pubic bone.

white blood cell count 10,800 per cubic millimeter, and urinalysis gave negative results. Repeated urinalysis showed strands of mucoid material, a rare granular cast, and a few motile bacteria. Urine culture revealed Aerobacter.

X-ray examination of the pelvis and of the left hip revealed no abnormalities (Fig. 1). Because of pain and spasm in the area of the left hip, a course of penicillin was started with a provisional diagnosis of acute arthritis or osteomyelitis in the left hip joint. A "scout" film of the abdomen made the following day showed slight intestinal ileus and a distended bladder. Two days later, the left hip could not be moved, since the child became extremely adverse to examina-

tion and defended himself against any movement whatsoever. Three days later, a barium enema and intravenous pyelography were performed, and these failed to show any abnormalities of the lower gastrointestinal tract or of the genitourinary tract. However, some osteoporosis of the pubic rami was visible for the first time. Repeated x-ray examination of the pelvis (Fig. 2) showed rapidly progressing destruction of the bone about the symphysis; at this time the diagnosis of osteitis pubis was made. Eleven days after admission an aspiration of the left pubic

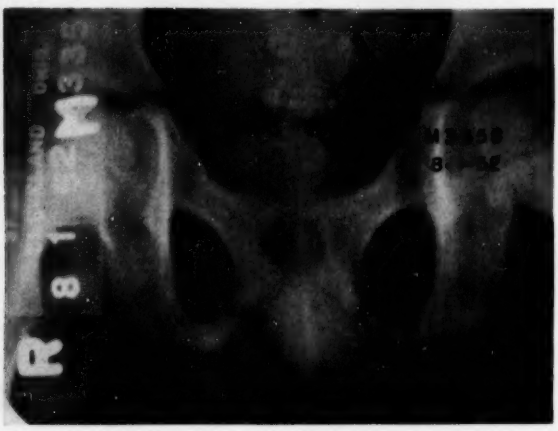

Fig. 3.—Progressive destruction of the bodies of the pubic bone at the symphysis.

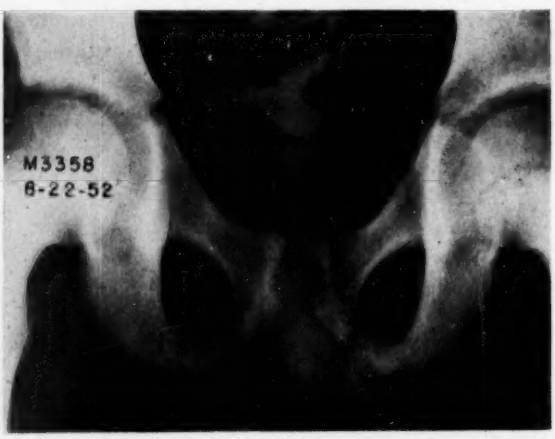

Fig. 4.—Beginning sclerosis at the margins of the symphyseal defect.

bone was performed with a Türkel trephine, and small amounts of material were obtained. Smears were inconclusive. No eosinophiles or granuloma cells were seen. A culture of the aspirated material showed no growth.

Within 13 days, the child was beginning to show clinical improvement, even though the x-ray evidence continued to show extension of the osteolytic process (Fig. 3). By the 19th hospital day, there remained only slight tenderness over the symphysis, and bed rest was no longer necessary. Clinical improvement continued steadily, and the child was discharged, symptom-free, on the 30th hospital day. Throughout the hospital course, the temperature curve

was essentially normal. Subsequent white blood cell counts varied from 5,200 to 7,000 per cubic millimeter, with normal differential patterns. Erythrocyte sedimentation rate, initially 32 mm. per hour, gradually fell to 8 mm. per hour upon discharge. Tuberculin test with purified protein derivative (P.P.D.) in the first and second strengths was negative. A sickle cell preparation was negative. Urinalyses were within normal limits. During his hospital stay, the patient received a total of 17,700,000 units of penicillin procaine.

Fig. 5.—Further healing of the bone lesions at the symphysis with increased area of sclerosis.

Fig. 6.—Regeneration of the bone at the symphysis almost complete.

Subsequent x-ray studies showed progressive healing, reaching complete resolution (Figs. 4, 5, and 6) eight months later. The patient has remained free from symptoms to the time of writing.

COMMENT

It is apparent that osteitis pubis may be considered a clinical entity, the clinical course, symptomatology, x-ray findings, and prognosis having a common pattern, although the cause is not known. Trauma, infection, or a combination of both have

been implicated as etiological factors. Infection has been thought to cause osteitis pubis, and cultures of Pseudomonas aeruginosa, Bacterium coli, Bacillus proteus, and Proteus vulgaris, all organisms of low virulence and low pathogenicity, have been reported. Lavalle and Hamm [6] obtained tissue studies from three autopsied cases and found, in two cases, pure cultures of Pseudomonas aeruginosa and one mixed culture of Pseudomonas aeruginosa and Proteus vulgaris. It is questionable that these Gram-negative bacteria are the etiological factors. Wheeler [11] could not produce osteitis pubis in rabbits by injection of infected urine into the bones or into the retropubic spaces. Osteitis pubis has been likened to Sudeck's atrophy and, in many respects, there are similarities. However, clinically, immobilization of the affected structures aids osteitis pubis, whereas in Sudeck's atrophy the symptoms are aggravated. No trophic changes are found over the pubes or soft tissues, as might occur in Sudeck's atrophy.

At first it was thought that opening the prevesical spaces with avulsion of the fibers of the rectus muscle or transversalis fascia at the attachment to the pubic bone was essential. In enucleation of the prostate, the puboprostatic ligament is often ruptured. Beer felt that it was a mild infection secondary to a bladder operation, possibly developing in the periosteum as a result of traction on the attached rectus muscles or due to direct bruising of the periosteum. Beach [1] noted that the bone lesions appear early near the location of the nutrient foramina and blood vessels and believed that infection spread by direct extension behind or through the foramina or as small emboli. Emboli of the obturator vessels would produce avascular necrosis, and trauma would produce vasoconstriction. Both processes are incompatible with the decalcification that occurs. The onset of rapid decalcification demands a marked hyperemia in the bones. Interference with the nerve supply to the blood vessels could cause the required hyperemia, but no verification of this hypothesis can be found. Rarely, vitamin or hormonal upsets have been thought to produce a similar condition. Unlike osteomyelitis in other locations, the onset of symptoms is abrupt, and pain, muscle spasm, and evidence of bone destruction occur almost simultaneously, without evidence of local swelling, lymph node enlargement, fistula formation, periosteal reaction, or sequestration. The patient improves clinically long before bone healing is completed.

Structurally, the disease may vary from a periostitis to extensive lesions of bones, with necrosis of cartilage and bone followed by subsequent healing and, infrequently, by hyperostosis. Microscopically, there is subacute inflammatory infiltration and chronic infiltration involving the periosteum, bone, and cartilage. Plasma cells, eosinophiles, and granulation tissue are found in the inflammatory tissue. The nerves show advanced degenerative changes and proliferation of the sheath cells. Fibrosis occurs in the marrow spaces. Granulation tissue is found on the outer surfaces of tendinous insertions, away from the bony insertions.

As yet, no specific method of treatment has been found. Sulfonamides and other antimicrobial agents seem to be of no avail, although some feel that penicillin shortens the clinical course. Bed rest is paramount, and, in the severer cases, immobilization with plaster jackets or traction frames may be necessary. Dean [6] feels that corticotropin (ACTH) decreases the demand for opiates markedly. Radiotherapy, diathermy, and radiant heat have been used to alleviate the symptoms. Vitamin B has been given, but the results are not impressive. Nerve root

block to control adductor spasm has been advocated, but paralysis of the abdominal muscles results. Recently, section of the obturator nerve has been attempted with favorable response.[10] In the main, the treatment is subjective at best, with relief of pain and avoidance of complications the object.

SUMMARY

Osteitis pubis is a rare clinical entity occurring post-traumatically and manifesting itself by severe pain over the area of the pubic symphysis, painful micturition and defecation, and painful pseudoparalysis. It is a self-limited disease, and complete resolution occurs within a year.

A case of osteitis pubis in a 6-year-old Negro boy is presented. Symptoms, pathologic anatomy, cause, and treatment have been discussed.

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"IDIOPATHIC" RUPTURE OF THE STOMACH IN A NEWBORN INFANT

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IN A REVIEW of the literature concerning rupture of the stomach in the newborn infant, Herbut [1] found 15 cases occurring prior to 1943 and reported a 16th case. Since that time, additional cases have been reported by Pendergrass and Booth,[2] Burnett and Halpert,[3] Tudor,[4] Wright and Scott,[5] Leger and co-workers,[6] Gottlieb and co-workers,[7] Ross and co-workers [8] (2 cases), Potter [9] (3 cases), and Greene and Gose [10] (2 cases), bringing the total of reported cases to 29.

The most frequent cause for the rupture would appear to be peptic ulceration. Thus, in 14 of the cases cited by Herbut and in 5 cases reported since that time,* the rupture was believed secondary to peptic ulceration. One of these [7] was associated with intracranial hemorrhage. In three cases,† a congenital defect in the musculature of the stomach was believed responsible for the rupture, and in one case,[3] pyloric atresia was present in addition to a congenital muscular defect. In one instance,[10] duodenal atresia alone apparently accounted for the rupture. In the remaining five cases,‡ no definite cause for the perforation could be established.

The present report concerns a case in which necropsy revealed no peptic ulceration, no defect in the gastric musculature, and no other abnormality which might account for the perforation. It is of some interest that the infant concerned had not been subjected to tracheal aspiration or feeding by gavage, procedures which have been thought [9] to be causative factors in rupture of the stomach. There would appear to be a small group of cases of rupture of the stomach in the newborn infant which must as yet be classified as "idiopathic."

REPORT OF A CASE

An infant girl, D. P., was born at 8:27 a. m. on June 30, 1953, the second child of young Negro parents. The family history was not remarkable, and there was no history of hypertension, toxemia, contagious illness, or other maternal abnormality during the period of gestation. The Rh blood type of the mother was positive and a serologic test for syphilis, negative. During labor, no medications were administered, with the exception of 100 mg. of meperidine (Demerol) intramuscularly three and one-half hours prior to delivery. After a labor of six and one-half hours' duration, "saddle block" anesthesia was induced, and the delivery was assisted by the

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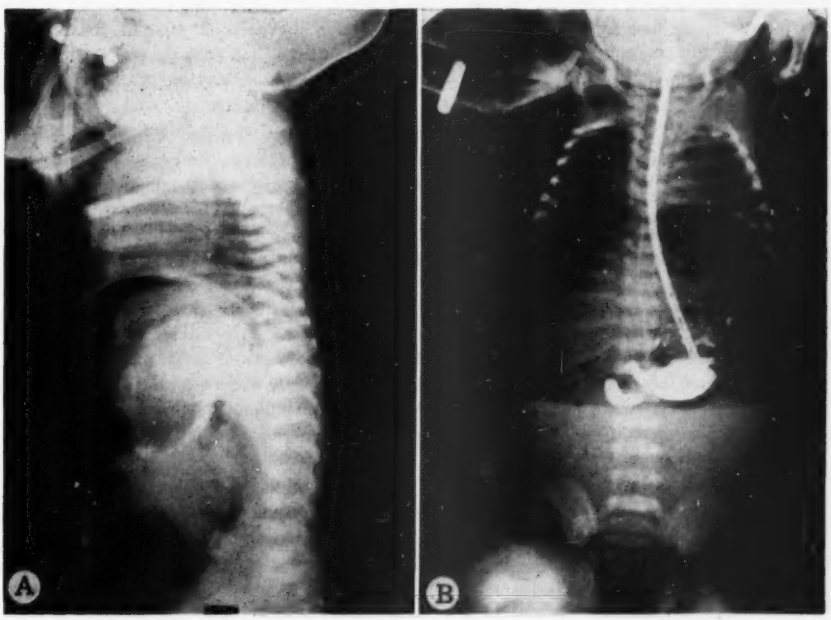
* References 5, 7, 9, and 10.

† References 1, 8, and 9.

‡ References 1, 2, 4, 6, and 8.

application of low forceps. At the time of delivery, the condition of the infant seemed good, the cry was lusty, and no abdominal distention or other abnormality was noted. The birth weight was 2,700 gm. Tracheal aspiration was not performed, and no gavage feedings were given. A 5% solution of Dextri-Maltose was fed at 4-hour intervals during the second 12-hour period following birth. Twenty-four hours after birth, the bassinet was moved beside the bed of the mother, and thereafter the infant was cared for by her mother. Feedings, consisting of a formula of evaporated milk and Dextri-Maltose, were taken well and retained until 8 a. m. on July 2 (48 hours after birth), but further feedings were refused. During the morning, the infant had a small normal bowel movement, and, except for some fussiness, her behavior did not seem unusual. She slept quietly during the afternoon, and urine was passed on four occasions. Physical examination at 8 p. m. revealed a quiet newborn infant who appeared to be in no severe distress and did not seem seriously ill; however, the abdomen was greatly distended and the overlying



A, Plain film of the abdomen in the right lateral projection. Note the sharp delineation of the abdominal viscera provided by the air anteriorly acting as a contrast medium. The diaphragms are elevated, and the abdominal wall protrudes anteriorly. *B*, Upright film of the abdomen in the anteroposterior position after the instillation of opaque material (iodized oil) through a catheter into the stomach. An air-fluid level is clearly illustrated at the level of the third lumbar vertebra, consistent with the presence of hydropneumoperitoneum. Mottled densities are seen in the left side of the abdomen, from the level of the 9th to that of the 12th rib, posteriorly, having the appearance of opaque material which has extravasated into the peritoneal cavity.

skin tight and shiny. No organs or masses were palpable, and peristalsis was not audible. Digital examination of the rectum failed to disclose any abnormality, and no feces were present on the examining finger.

Roentgenographic examinations disclosed normal lung fields. Films of the abdomen (Figure) demonstrated a large semilunar area of radiance anteriorly having the characteristic appearance of free air in the peritoneal cavity. Films taken in the erect position clearly demonstrated an air-fluid level. After introduction of iodized oil into the stomach, opaque material was

visualized in the distal portion of the stomach and in the duodenum. More mottled, scattered accumulations of opaque material were seen in the left upper abdomen, consistent with extravasation of the oil into the peritoneal cavity.

An exploratory laparotomy was performed between 2:20 and 3:20 a.m. on July 3, 1953. Anesthesia consisted of local infiltration with 0.75% procaine solution, supplemented with inhalations of a mixture of equal parts of nitrous oxide and oxygen. The peritoneal cavity was entered through a high right rectus incision, and large amounts of air, purulent fluid, and milk curds were drained from the abdominal cavity. No fecal odor was present. From the surface of the bowel and from pockets between the loops of the bowel, yellowish bits of necrotic material measuring 1 to 2 cm. in length by 2 to 4 mm. in width were removed. A defect was found in the superior one-third of the anterior wall of the stomach, measuring approximately 2 cm. in length and 2 mm. in width and surrounded by an area of black necrotic tissue, extending 2 mm. from the edges of the defect. Adequate exposure of the defect was obtained with difficulty because of the location, but closure was accomplished with a continuous 00 chromic absorbable surgical (gut) suture, the necrotic edge of tissue being inverted into the stomach. When the stomach was permitted to fall into normal position, the closed defect was found to lie against the diaphragm and the surface of the liver. No abnormality of the duodenum or small bowel was noted. During the operation, respirations ranged between 40 and 60 per minute and the general condition of the infant appeared good.

No oral fluids or medications were administered. Fluids given intravenosuly during the 29 hours following the operative procedure totaled 305 ml., including 30 ml. of whole blood. Penicillin procaine, in a dosage of 100,000 units daily, and streptomycin, 25 mg. every six hours, were administered intramuscularly, beginning immediately after the completion of the operation. Vitamin K and vitamin C were given intramuscularly in doses of 2 mg. and 50 mg., respectively. The temperature rose to 101 F. after the operation; then it fell rapidly and remained between 95.6 and 97 F. Respirations continued to be rapid, ranging between 40 and 60 per minute. The cry was rather weak, but the general condition otherwise seemed fairly good. Urinary output remained adequate. Small yellow stools were passed at 4 a.m. and at 7 a.m. on July 4. At 8:30 a.m., the respirations suddenly became wheezing in character and associated with subcostal retraction and abdominal distention. No cyanosis was evident. At 9:15 a.m., the respirations suddenly ceased, and heart tones could not be heard. At 9:20 a.m. on July 4, the infant was pronounced dead.

Necropsy was performed at 10:30 a.m. on July 4, and pertinent findings were as follows: No rigidity was present, and there was no evidence of postmortem decomposition. Length was 41 cm. and weight 2,470 gm. Nutrition was that of a normal newborn infant. A recently closed incision measuring 6 to 7 cm. in length was present along the upper portion of the lateral border of the right rectus muscle. The subcutaneous adipose tissue was between 2 and 3 mm. in thickness. When the peritoneal cavity was opened, approximately 30 ml. of dark red-brown fluid gushed forth. All the peritoneal surfaces, including the liver, spleen, genital organs, bladder, and intestines, showed a yellow, plastic, partially organized exudate. Culture of the peritoneal surfaces revealed the presence of abundant growth of slightly hemolytic Escherichia coli and a few colonies of gamma streptococci. The intestinal tract was not distended. The leaves of the diaphragm were at the level of the fourth intercostal spaces. The pleural cavities were free of fluid and adhesions. The left and right lungs weighed 17 and 16 gm., respectively, and were of normal appearance. Microscopic examination revealed minimal pulmonary atelectasis. There was no evidence of pulmonary edema. The heart weighed 14 gm., and no abnormality was disclosed by gross or microscopic examination. The liver weighed 100 gm. and, other than the yellow fibrinous deposits on the surface, showed no abnormality grossly or on microscopic section. The stomach appeared normal in size, measuring 4 to 5 cm. along the lesser curvature and 9 to 10 cm. along the greater curvature. Patches of yellow fibrinous exudate were seen on the anterior surface. An oblique suture line in the superior one-third of the anterior wall of the stomach extended 2 cm. inferiorly and to the right from a point located approximately 0.5 cm. from the greater curvature and 2 cm. from the cardia. No separation of this suture line was evident, and

healing appeared to be occurring. The stomach contained approximately 35 ml. of gas and 5 ml. of yellow-white, pasty material. No ulceration of the gastric mucosa was disclosed by microscopic examination, and the muscularis was seen to extend to the site of the rupture. There was no microscopic defect in the suture line. Beneath the mucosa and in the serosa in the region of the rupture were numerous capillaries, thin-walled blood vessels, and marked fibroblastic proliferation, but no evidence of intramural hemorrhage. Many polymorphonuclear leucocytes, much amorphous fibrinoid material, and small hemorrhages were also evident in the serosa. The pylorus and duodenum showed no evidence of obstruction or other abnormality, and the remainder of the intestinal tract was normal, except for the serosa, which showed fibrin deposition, as mentioned previously, and moderate hyperemia.

COMMENT

It would appear that rupture of the stomach in the newborn infant is most frequently caused by peptic ulceration. In this regard, Potter [9] has stated:

> Rupture of the stomach . . . is most often observed in infants who have been fed by gavage and the site is frequently the greater curvature of the stomach in the region most susceptible to damage from introduction of a gavage tube. It is also possible that accidental introduction of a tracheal catheter into the esophagus and stomach during attempts at resuscitation may produce injury. It seems probable that in most instances the mucosa is traumatized, infection sets in and perforation follows.

Because of the general belief that rupture of the stomach in the newborn infant is almost uniformly secondary to perforation of a gastric ulcer, it is of considerable interest that ulceration was found in only 4 of the 14 cases reported during the last 11 years. It is possible that physicians encountering gastric perforation due to causes other than ulceration have been more prone to report their cases because of the apparently unusual etiology. On the other hand, in some of the early reports the appearance of the lesion at the time of necropsy was not recorded in detail, and one wonders whether evidence of ulceration was definite, or whether, in the absence of other apparent cause, perforation was merely assumed to be secondary to ulceration.

In one of the cases described by Ross and co-workers,[8] it was felt that an intramural gastric hemorrhage might have been the cause of the rupture. The cause of the intramural hemorrhage was not determined, and other evidences of an abnormal bleeding tendency were apparently not present. In the case reported here, intramural hemorrhage was not present.

SUMMARY

A case of rupture of the stomach in a 3-day-old infant is reported. Necropsy failed to reveal any cause for the perforation.

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Progress in Pediatrics

DIAGNOSIS AND SURGICAL MANAGEMENT OF OBSTRUCTIVE UROPATHY IN CHILDHOOD

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AND
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OBSTRUCTION at the outlet of the urinary bladder is commonplace in senescent men, and physicans in general are aware of its frequent occurrence and are alert in recognizing it. Yet the occurrence of similar obstructive uropathy in children is less understood by the medical profession, with the result that physicians and parents alike often overlook certain abnormalities of micturitional behavior in infancy which if recognized would lead to early discovery. For the male normally urinates a forceful high trajectory stream, which is at once the object of curious pride to his mother as well as the envy of his male parent, and he empties his bladder with a continuous stream. Any male infant who does not emulate the boy made famous in the statue in Brussels and who urinates with an interrupted stream must be regarded with grave suspicion. Such a child probably has an impediment to the natural evacuation of his bladder, and, if this is allowed to progress untreated, may develop irreparable damage to the upper urinary tract.

Doctors routinely instruct mothers of newborn babies regarding the care of their infants and inform them about certain observations that should be made from time to time, for example, bowel habits, sucking techniques, etc. Equally important should be the observation of the act of urination. Any evidence of impediment should prompt early investigation. One of us read a short report on this subject a few years ago, which was published in the *Journal of the Michigan State Medical Society*. A few months later, he received a phone call from a physician in a nearby city who reported that his daughter-in-law and grandson were staying with him for a short time waiting the day of departure for Japan, where the doctor's son was in military service. Having recently read the article in question, the grandfather observed the infant void and was impressed by the degree of hesitancy and the interrupted nature of the child's stream. His anxiety led to an investigation which revealed the presence of obstructing valves in the urethra and the presence of residual urine amounting to 100 cc. The obstruction was easily corrected, and within a short time the infant was voiding freely and without interruption. The mother and child were able to fly on schedule to be with the father.

The symptoms that usually call attention to these disorders are likely to be the result of advanced complications of urinary obstruction. Thus, loss of appetite and apathy associated with uremia may cause the parents of a child to seek medical advice. More frequently the presenting complaint is recurrent urinary infection that fails to respond permanently to any form of antibacterial medication, for obstruction enhances persistent infection, especially when there is residual urine. Troublesome enuresis in some instances will be found to result from obstruction

and associated residual urine, and urinary incontinence by day is often the result of an advanced stage of this condition. When complete decompensation of the bladder musculature has occurred, there may be an abdominal mass present which erroneously can be interpreted as the usual potbellied configuration of a child of this age. As the present report is being written, a 7-year-old boy with this condition has been admitted for observation in the University Hospital. His kidneys and ureters are dilated beyond hope of recovery. His mother states that she took the boy to a local physician at the age of 2 years because he had a protuberant abdomen and often wet himself during the day as well as at night. The physician examined the child and informed the mother that the boy was normal, but she was not reassured, so consulted a "specialist," who also found no cause for concern. In retrospect, it seems likely that the protuberance five years ago was due to bladder distention and that diagnosis then might have resulted in salvage of a condition now hopeless.

Indeed, the well-baby clinic is the first line of attack in the early recognition of obstructive lesions which if left alone and unrecognized will eventually result in permanent damage to the urinary tract.

What are these obstructive lesions? The scope, while not broad, includes both rare and ordinary lesions and must take into account acquired as well as congenital defects. For purposes of clarity, the following brief discussion of the commoner varieties encountered will be based on the anatomic order of their occurrence, from the urethral meatus to the bladder neck.

MEATAL STRICTURE

Congenital imperforate urethra occurs infrequently. Its detection is not long delayed, for a persistently dry diaper is quickly brought to the attention of the physician by the attending nurse or the mother of the child. Congenital narrowing of the urethral meatus is far commoner. It, along with acquired reduction in meatal caliber such as might occur after diaper meatitis in the recently circumcised baby or follow chronic balanitis in the uncircumcised phimotic boy, is less likely to be quickly recognized. The adverse changes induced by this apparently simple lesion, whatever its cause, are nicely illustrated in the case of a 2-month-old infant brought to University Hospital because of an enlarged misshaped phallus. Inspection disclosed a redundant prepuce with phimosis (Fig. 1). The pendulous urethra appeared dilated and doughy in consistency. On compression of the shaft, urine could be expressed from the phimotic orifice. A urethrocystogram disclosed a relaxed, capacious, pendulous, and bulbar urethra (Fig. 2). After dorsal slit of the prepuce, a congenitally narrowed urethral meatus was discovered. A meatotomy was performed (Fig. 3), and this was followed by a suprapubic cystotomy, done to provide drainage until return of kidney function would permit additional investigation and probable plastic reconstruction of the penis and urethra.

A similar case (Fig. 4), represented only by a cystogram, shows an advanced stage of obstructive uropathy secondary to meatal stricture. This patient at the age of 32 years shows massive reflux of radiopaque material injected into his bladder completely outlining a vastly dilated upper urinary tract.

The performance of meatotomy with subsequent dilatation of the meatus with a bougie for the following two to three days to prevent healing at the original small

caliber is all that may be required when the lesion is discovered early. Circumcision in chronic recurrent balanitis and correction of diaper irritation are necessary accompaniments if these factors are present and predispose to perpetuation of the process. Diversion of the urinary stream by cystotomy is seldom necessary and is

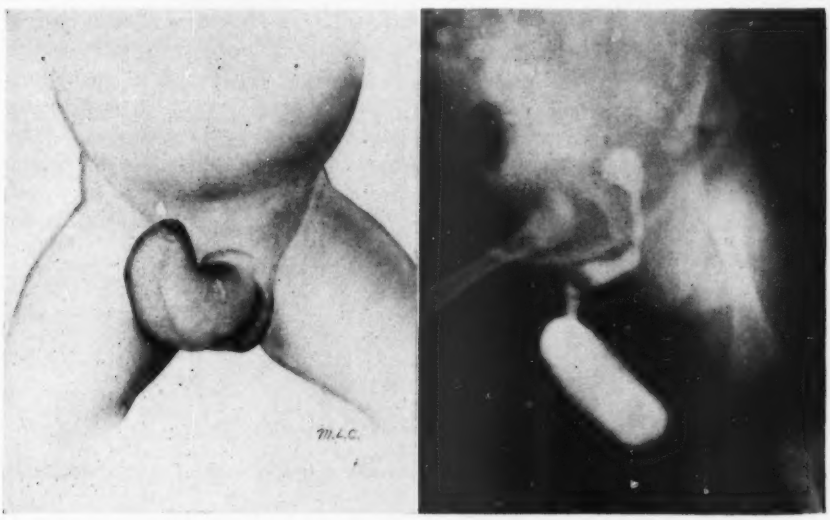


Fig. 1.—An enlarged misshaped phallus and redundant prepuce with phimosis in a 2-month-old infant.

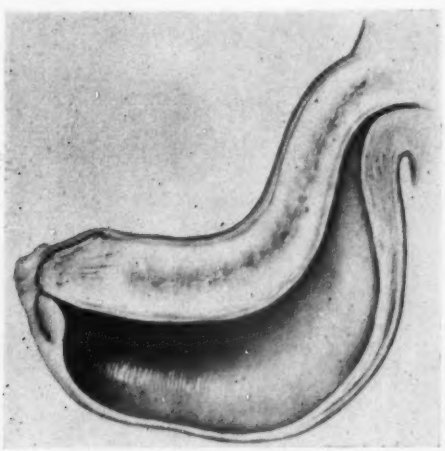


Fig. 2.—A relaxed, capacious, pendulous, and bulbar urethra in a 2-month-old infant.

reserved for those cases where extensive renal damage can be demonstrated by cystography and pyelography and where restitution of kidney function is an obvious necessity before further investigation or definitive corrective procedures can be carried out.

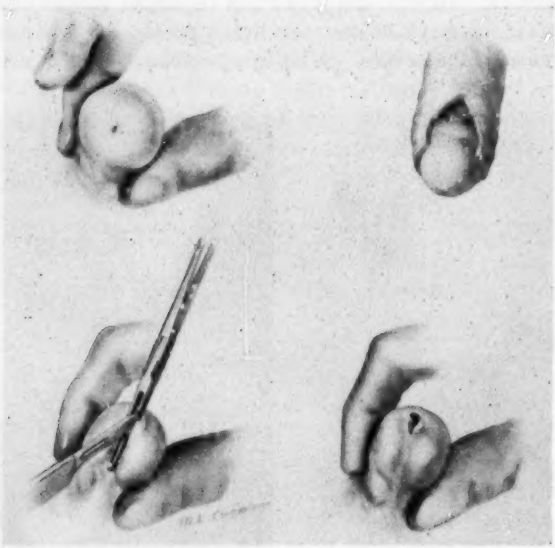


Fig. 3.—A meatotomy performed on a congenitally narrowed urethral meatus, discovered after dorsal slit of the prepuce.

Fig. 4.—Cystogram showing massive reflux of radiopaque material injected into the bladder, completely outlining a vastly dilated upper urinary tract.

CONGENITAL URETHRAL VALVES

The prostatic urethra may be the site of a variety of obstructive anomalies. Congenital urethral valves are found in this region. Some are filamentous or veil-like and, while attached to the surrounding tissues, seem quite different in character from the mucosal structures to which they adhere. Others take on the character of deep folds or redundancies and appear continuous with the bladder and urethral surfaces. Both groups are usually attached at one end to the verumontanum. McKay and Young have classified valves into three types (Fig. 5): (1) the membranes extend from the verumontanum toward the external sphincter; (2) the filaments extend back toward the vesical neck, and (3) the membrane extends across the urethra like a diaphragm. Perhaps a fourth category might be added, since frequently the valves may coexist with hypertrophy of the verumontanum itself. The verumontanum may assume an elongated or polypoid appearance and thus act as a ball

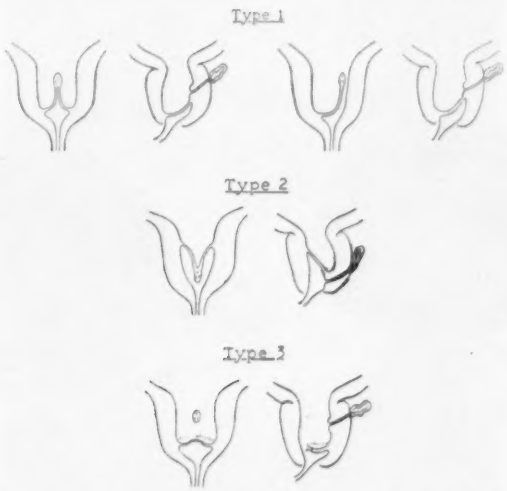
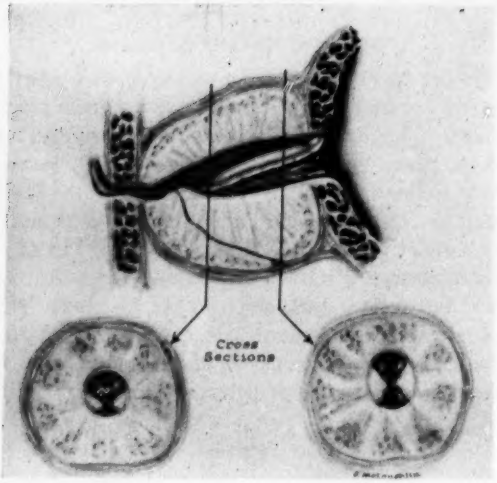


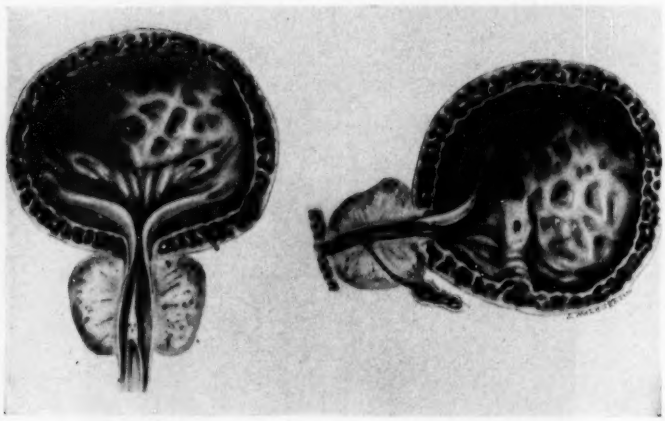
Fig. 5.—The three types of congenital urethral valves, as classified by McKay and Young.

valve. Several of these varieties are illustrated in drawings made from three cases recently observed at the University of Michigan (Fig. 6).

If congenital urethral valves are suspected on the basis of existing signs and symptoms, additional diagnostic procedures may be employed to substantiate this impression. If renal function is sufficient to allow concentration of intravenously administered contrast medium, the status of the kidneys may be easily determined by pyelography. This alone may not suffice, for often intravenous pyelograms may appear quite normal, yet the cystogram (Fig. 7) performed with delayed exposures will show reflux of radiopaque material into the upper urinary tract. Of course, even without roentgenographic aids, considerable information may be secured by the introduction of a catheter after micturition into the bladder in order to determine the presence or absence of residual urine.

None of these techniques actually establish the diagnosis but only hint at its presence. Instrumental examination with the endoscope may supply the additional





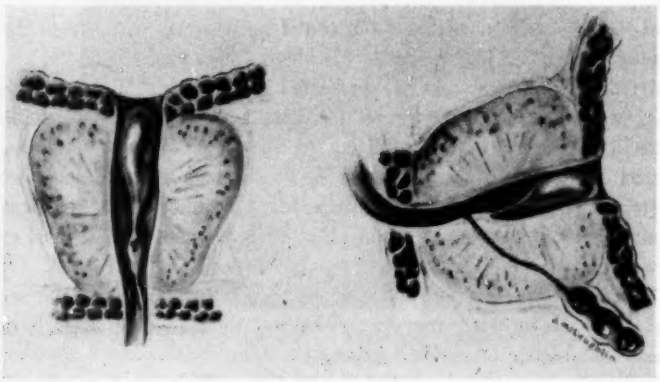


Fig. 6.—*A*, congenital valves of the prostatic urethra; *B*, redundant mucosal flap of the vesical neck; *C*, polypoid lesion within the prostatic urethra.

data needed. Such an examination is not without danger, however. The small urethra of infancy does not lend itself well to manipulation with a rigid device. The examiner is further hampered by visual and mechanical limitations imposed by an instrument of 12 F. caliber or less. Despite these drawbacks, such an examination is possible. In fact, in 22 of the last 23 substantiated cases at the University Hospital, diagnostic endoscopic inspection of the urethra was accomplished. In three of these cases, a perineal urethrotomy was performed to facilitate introduction of the instrument and thus avoid trauma.

Perhaps from the preceding discussion it might be assumed that instrumentation for purposes of diagnosis is regarded as routine. A word of warning in this

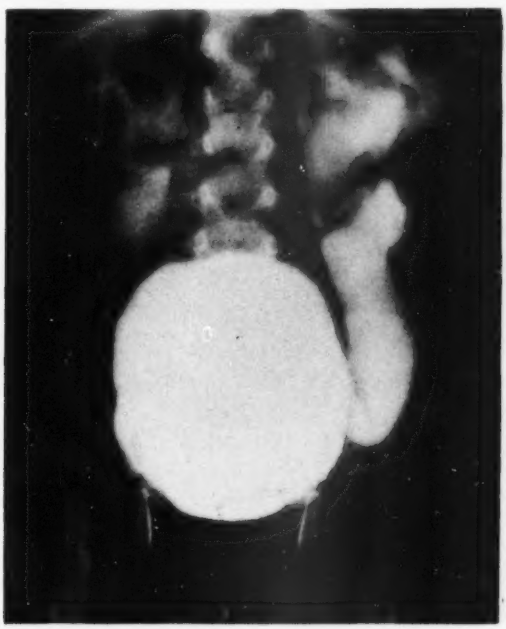


Fig. 7.—Cystogram performed with delayed exposures, showing reflux of radiopaque material into the upper urinary tract.

regard may not be out of place. The child possessed of congenital urethral valves is frequently presented to the physician in what may appear to be reasonably good condition when in actuality his internal chemical environment is being maintained virtually on the brink of ionic disaster. If this anemic azotemic acidotic infant has introduced into the sterile cavity of his bladder a catheter or instrument with the inevitable accompanying bacterial invader, and if this catheter is then withdrawn, the organism may multiply in the most ideal of all culture media, namely, static urine, and may choose to ascend the adynamic ureters and impose itself on an already weakened kidney, with inevitable pyelonephritis.

What conclusions may be drawn from this? Certainly, selected preliminary determinations of the chemical constituents of the blood should precede other diag-

nostic efforts. If the patient is in obvious jeopardy, then immediate suprapubic cystotomy will suffice to establish needed drainage with the least amount of trauma and danger to the patient. All efforts may then be directed to the immediate problem at hand, the correction of chemical imbalance and restoration of homeostasis.

If such preliminary investigations indicate satisfactory renal function, or if the performance of cystotomy is followed by reasonable restitution of kidney function and return of bladder tone, then definitive correction of the primary abnormality is the next logical step. The recent development of a transurethral resectoscope of infant size has enabled the urologic surgeon to correct this abnormality by excision of the valves under direct vision, an advantage not shared by the perineal and suprapubic approaches, the use of blind sounds, or the inaccurate application

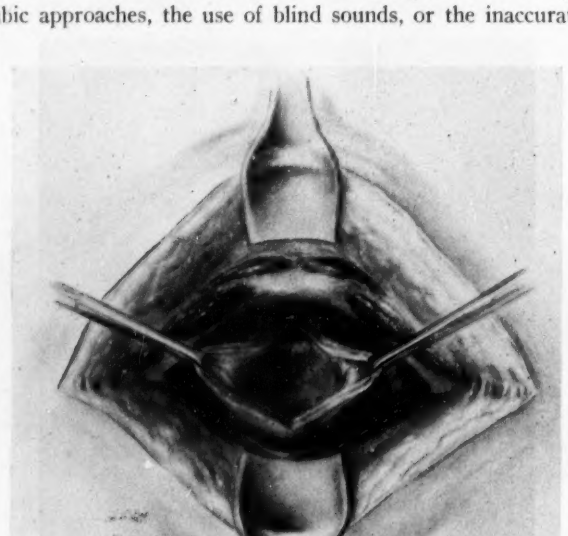


Fig. 8.—Retropubic exposure of the prostatic urethra.

of fulgurating electrodes through the endoscope. Nevertheless, even those skillful in the manipulation of this instrument will admit that its size at times proves too great a barrier to accurate direction of the cutting electrode and that, in addition, there are those cases where it is actually impossible to introduce the instrument, even by urethrotomy. This is especially true of the very young patient and, of course, leaves cystotomy as the only alternative. Such a choice might be avoided if some other approach were reasonable. The answer may perhaps be found in the application of the technique of retropubic exposure of the prostatic urethra to the child (Fig. 8). Many surgeons have found that the visual picture it affords the operator is unexcelled. The prostatic urethra of the infant is even more accessible by this method than is that of the adult, and, in addition, there is the advantage of fewer blood vessels to interfere with exposure. Actual sharp dissection of the

valves from their attachments to the bladder, urethra, and verumontanum, primary suture of bleeding points, and freedom from the adverse effects of thermal coagulation are additional benefits which favor this method.

VESICAL NECK CONTRACTURE

Contracture of the vesical neck is another congenital anomaly whose presence is seldom suspected. In its childhood form it is histologically characterized by a local increase in connective tissue of the submucosa. The distribution of this tissue is such that the neck of the bladder tents up to form a median bar, with a cavity on each side representing the prostatic fossa distally and the bladder cavity proximally. The bladder falls away into a deep recess, or bas-fond, whose only elevation may be the plateau formed by a hypertrophied trigone. The introduction of a panendoscope into the urethra will readily establish the diagnosis. In addition to the median bar, which acts as a deterrent to the passage of the instrument, the examiner will see the deep bas-fond beyond the lip of tissue at the vesical neck and the hypertrophied trigone, and if obstruction has not resulted in complete bladder decompensation he may see evidences of increased detrusor activity in the form of trabeculation of the muscular wall. Incompetency of the ureterovesical junction may be indicated by gaping ureteral orifices. Sometimes the cystoscopist can feel the snugness of the vesical neck on the instrument as it grips it very much like a tight urethral stricture on a steel sound, or, with one finger in the rectum, he may feel the collar-like ring of the vesical neck on the panendoscope. A cystogram, pyelograms, and studies of renal function will complete the picture.

Before institution of therapy, it is etiologically important to rule out disease of the central nervous system in these cases. A discussion of the controversial features of neuromuscular structure and function of the bladder neck is not indicated here. Suffice it to say that in certain disorders of the nervous system examiners have observed what appears to be muscular spasm or hypertrophy of the vesical neck. Whatever its origin, it may visually simulate the changes seen in certain stages of congenital vesical-neck contracture. A careful neurological examination, cystometry, and detailed neurologic x-ray techniques may aid in the differential diagnosis. This point is well illustrated by a recent case on an 8-year-old boy with enuresis and urinary tract infection who was found on cystoscopy to have a vesical neck contracture and a measured urinary residual of 150 cc. Neurologic examination disclosed upper motor-neurone involvement, with pyramidal tract signs, and lower motor-neurone involvement, with unilateral saddle anesthesia. Cystometry demonstrated an uninhibited neurogenic bladder; spine films disclosed a spina bifida, and a myelogram revealed a tumor deformity confirmed at laminectomy. In such an instance, correction of the vesical-neck abnormality could at best be classed as an incomplete approach to the total problem.

In choosing a proper approach for the correction of vesical-neck contracture, the surgeon is beset by the same mechanical barriers already outlined in the consideration of surgery of congenital valves. In this instance, the nature of the tissue present offers an additional problem. As stated, the histopathology of congenital vesical-neck contracture is one of excessive connective tissue with round-cell infiltration. Transurethral resection of the obstructing element, contrary to the belief

of some, does not offer the ideal solution for the removal of this type of tissue. While this is almost uniformly successful in the immediate creation of a more adequate outlet, with relative freedom from trauma, blood loss, and the delay necessitated by the healing of an open wound, the long-term results, as indicated by follow-up examinations, are not satisfactory, for recurrence of the contracture is common. For this reason, surgeons have come to rely again on the advantages offered by the retropubic exposure of the vesical neck (Fig. 9). The goal in this instance is

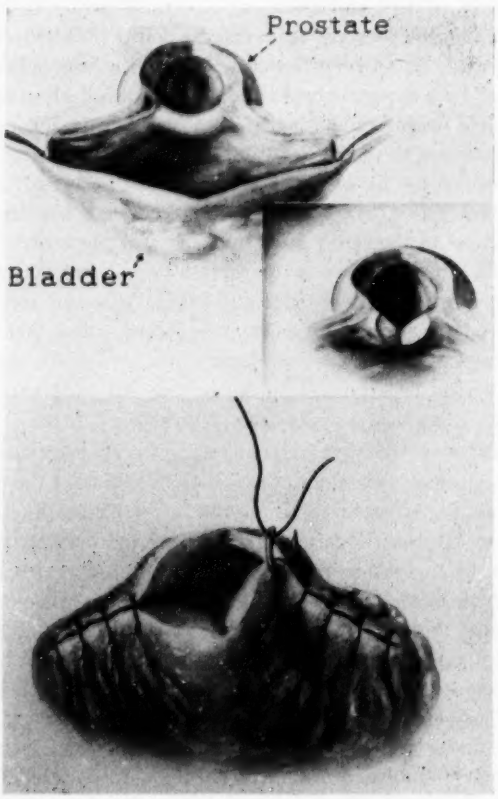


Fig. 9.—Retropubic exposure of the vesical neck, with section of the contraction ring and cystorrhaphy to widen the orifice.

not only a section of the contraction ring, but also a cystorrhaphy to widen the orifice. Dr. Bradford Young has recently reemphasized the benefits of a vertical incision over the prostatic urethra, extending into the bladder neck. The exposure of bladder and prostatic cavities is thus easily accomplished, a wedge removed from the bladder neck by sharp dissection, the defect covered with mucosa, and, probably the most important step of all, the vertical wound then closed transversely, as might be done in a pyloroplasty. This widens the vesical orifice appreciably and mitigates against recurrence of the original problem.

HYPERTROPHY OF THE VESICAL NECK

Closely related to vesical-neck contracture is another entity, considered to be rare, but perhaps, in retrospect, far commoner than is presently appreciated. Its clinical course is nicely illustrated by a 7-year-old girl admitted to the University Hospital for consultation. Her referring physician, a competent urologist, had treated her intermittently over a three-year period for recurrent lower-urinary-tract infection. During the initial phase of her investigation, cystoscopy was carried out, and pyelograms were made to rule out factors likely to contribute to the perpetuation of the process. None were found. The bladder was of normal capacity, its wall was smooth, and no residual urine was discovered. The vesical outlet was considered adequate. Three years later, discouraged by the persistent intermittency of this child's cystitis, the same urologist again did cystoscopy and on this occasion found residual urine of 160 cc. Instead of a smooth-walled bladder, there was now

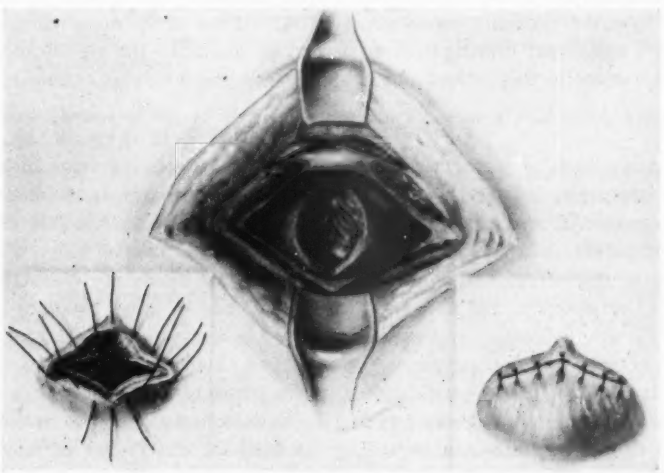


Fig. 10.—Retropubic exposure of the vesical neck.

gross trabeculation and a definite increase in total capacity. Pyelograms were still normal. The vesical outlet was considered adequate. Surprised by this obvious change in appearance with the passage of time and with no apparent reason for the change, the physician sought an additional opinion. The admission examination at University Hospital added no other information. There was no measurable neurologic deficit either on cystometry or on detailed neurologic tests. The child carried 160 to 180 cc. of infected residual urine after voiding without appreciable effort. Repeat cystoscopy showed the changes already described. At first glance, the vesical neck appeared quite adequate. However, on further visual evaluation, it seemed as if there might be some encroachment of the outlet laterally and superiorly on withdrawal of the instrument.

Because of these findings, the obvious progression of signs and symptoms, and the fear that continuation would eventually result in involvement of the upper urinary tract, it was decided to expose the vesical neck by the retropubic route.

This was done (Fig. 10). A vertical incision was made over the bladder outlet and an amazingly thickened musculature encountered, at least 2 cm. in depth. The rest of the bladder by comparison seemed relatively normal or perhaps slightly thickened. Trabeculation was seen. The vertical wound was closed transversely, and a catheter was left in the urethra for 10 days as a splint and to accomplish drainage and was then removed, with immediate return to normal urinary function. The patient emptied her bladder without residual urine, and after discharge from the hospital, returned for a check-up examination four weeks later with again no residual urine and, interestingly, no infection, despite the fact that no medication was given at the time of discharge.

Is hypertrophy of the muscle of the vesical neck a congenital obstructive disease, such as is seen in pyloric stenosis, or is the situation seen here a panoramic view of what may occur in many children with recurrent cystitis, namely, infection, irritation, and secondary vesical muscular spasm with partial obstruction, followed by hypertrophy, trabeculation, and then, later, decompensation, and residual urine followed by ureterovesical incompetency with dilatation of the upper urinary tract? Obviously, additional investigation is needed to ascertain the significance of the changes observed in this patient and in others seen under similar circumstances.

SUMMARY AND CONCLUSIONS

The association of obstructive uropathy with the senescent stage of existence has, unfortunately, led to the supposition that its occurrence in childhood is, by contrast, rare. All evidence points to the contrary. The inarticulate child, the untrained parent, and the unsuspecting physician may inadvertently allow perpetuation of this error. The child whose micturitional habits are characterized by hesitancy, infrequency, and a poor stream productive of small volumes of urine, or the child who is beset by enuresis, or who may be the victim of recurrent urinary-tract infection, while not necessarily possessed of obstructive disease of the lower urinary tract, is at least a candidate for investigation to rule it out.

A plea is made for physicians to include in their instructions to the parents of newborn children information regarding the need for observance of micturitional behavior. When this is not normal, an early investigation should be advised.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Alfred S. Traisman, M.D., President
Regular Meeting, April 20, 1954

Disseminated Lupus Erythematosus in Children. Dr. Melvin A. Krugly.

The diagnosis of disseminated lupus erythematosus has been made in children with greater frequency during the past few years. This paper is a report of six cases of disseminated lupus erythematosus treated on the pediatric ward of the University of Illinois Research and Educational Hospital. The clinical picture of these six patients is reviewed, pointing out the protean nature of this disease. Laboratory studies also demonstrate the diffuse involvement of renal, hepatic, hematopoietic and other organ systems. Both corticotropin (ACTH) and cortisone have been found to be effective in the therapy of this condition, and the use of steroids in the treatment of five of the children is briefly discussed, noting the changes which ensued in the clinical and laboratory findings.

Comparative Studies of Blood Methemoglobin in Premature Full-Term Infants and Children. Dr. L. D. Elegant.

It has previously been shown that methemoglobin may exist normally in small amounts in the blood of children and adults. The concentrations of methemoglobin in the blood sera of normal premature and normal full-term newborn infants were studied. The purpose was to determine whether any relationship exists between the methemoglobin levels and cyanosis, which is so frequently seen in these infants.

A modified method for determining methemoglobin levels was developed. The results were compared in these infants with results found in older children and adults. The results in the study were also compared with those of other investigators in older children and adults.

Normal premature infants were found to have significantly higher levels (four to five times as high) than those of older children and adults. Methemoglobin levels in normal full-term newborn infants were also found to be somewhat higher. No apparent correlation was found between methemoglobin levels and visible cyanosis.

The mechanism by which hemoglobin is oxidized to methemoglobin was discussed and a postulate advanced whereby the mechanism may be reversed in the premature infants.

Lead Poisoning in Children, Including Nine Cases Treated with Ethylenediaminetetraacetate (EDTA). Dr. Arnold L. Tanis.

A series of 33 patients in whom the diagnosis of plumbism was substantiated by history and laboratory examination is presented. Thirteen of these cases occurred in 1953.

The greatest incidence occurred between 1 and 3 years of age and included 70% of the cases. Seventy-eight per cent of the patients were admitted to the hospital during the hot summer months of June, July, and August. The total mortality was 18%.

The average duration of symptoms prior to admission was 4.8 weeks. The most common cause of lead poisoning in children is ingestion of paint. The symptoms are divided into major and minor complaints, with pica, paint ingestion, vomiting, irritability, constipation, listlessness, anorexia, abdominal pain, weight loss, and pallor comprising the major groups. Pica, or perverted appetite, was present in 93% of the cases and is emphasized and discussed. The minor complaints included convulsions, urinary difficulty, coma, stupor, ataxia, behavioral and mental changes, tremors, muscle weakness, and sleeping poorly.

An analysis of the source of the paint collected from the window sills and walls in the homes was made.

The physical, laboratory, and x-ray examinations were discussed, with special emphasis placed on the urinary excretion of lead and its importance in diagnosis.

There was a consistent pattern of abnormality in the electroencephalogram. This has not been described previously.

Differential diagnosis with common pitfalls was presented.

Therapy was discussed, and encouraging results utilizing the chelating agent etheylenediaminetetraacetate (EDTA) in nine patients in the series was emphasized. This is a nontoxic substance which mobilizes lead, forms a stable compound with it, and then is rather promptly excreted in the urine.

Mental development was represented in the follow-up care by psychometric tests.

The pathology was described briefly. The prognosis in lead poisoning, as well as in the more severe encephalopathy in children, must be guarded. There is a high incidence of life-long residual nervous-system injury.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

PYRIDOXINE DEFICIENCY IN THE HUMAN INFANT. SELMA SNYDERMAN, L. E. HOLT JR., R. CARRETERO, and KATHRYN JACOBS, J. Clin. Nutrition **1**:200 (March-April) 1953.

The authors review the available data on experimental pyridoxine deficiency in animals and in adult humans. They report observations on two mentally deficient infants (whose diagnoses included hydrocephalus and porencephalus) maintained on a pyridoxine-deficient diet for several months. The infants were 2 and 8 months of age, respectively, at the beginning of the study. The younger of the two subjects manifested failure to gain in weight after the 33d day of the experimental period and on the 76th day developed a generalized convulsion with loss of consciousness. Intravenous administration of 50 mg. of pyridoxine produced some improvement in three hours, followed by full recovery the next day. The other subject failed to gain in weight after the 73d day and developed severe microcytic hypochromic anemia by the 130th day of study. The anemia did not respond to iron therapy, whereas administration of pyridoxine produced a rapid response. This latter subject did not have convulsions.

Both subjects showed a marked drop in urinary excretion of pyridoxine hydrochloride and pyridoxic acid and an impairment in ability to convert tryptophan to N^1-methylnicotinamide. The latter is suggested as a possible test for pyridoxine deficiency in human subjects.

FORBES, Rochester, N. Y.

EFFECTS OF DIETARY TERRAMYCIN AND METHIONINE SUPPLEMENTS ON FAT AND PROTEIN GAINS IN WEANLING RATS. E. W. HARTSOOK and B. CONNOR JOHNSON, J. Nutrition **51**:205 (Oct. 10) 1953.

The authors found that with methionine and cystine at levels bordering on the inadequate, rats given such a ration supplemented with antibiotics had increased gains, such gains being largely fat. When adequate or excess methionine and cystine were present, the efficiency of dietary nitrogen utilization was increased and carcass fat deposition did not increase as fast as with the diet bordering on inadequacy with respect to these amino acids. The reason for the increased protein synthesis is not at present apparent, since the data obtained in this experiment show only that the interaction of additional methionine and oxytetracycline (Terramycin) resulted in more efficient utilization of the dietary nitrogen but did not differentiate as to the degree to which one substance enhanced the other.

FREDEEN, Kansas City, Mo.

LIBERATION AND MEASUREMENT OF PANTOTHENIC ACID IN ANIMAL TISSUES. B. S. SCHWEIGERT and BARBARA T. GUTHNECK, J. Nutrition **51**:283 (Oct. 10) 1953.

Schweigert and Guthneck determined the pantothenic acid content of composite samples of beef, pork, and lamb organs. Liver, kidney, and pancreas were shown to be the richest sources of pantothenic acid, heart and brain were intermediate, and lung and spleen were lowest in pantothenic acid content. The latter organs contained approximately twice the amount of pantothenic acid found in pork, beef, or lamb muscle cuts.

FREDEEN, Kansas City, Mo.

UNSATURATED FATTY ACIDS AND ALLOXAN DIABETES. RICARDO R. RODRIQUEZ, PEDRO CATTANEO, BERNARDO A. HOUSSAY, and BUMPEI UNO, J. Nutrition **51**:441 (Nov. 10) 1953.

The protective action of some fats against the toxic and diabetogenic action of alloxan seems to be related to the quantity of saturated fatty acids present in the fat used. This marked effect was observed not only in those rats fed saturated fatty acids which are poorly absorbed from the intestine, that is, in the animals fed a high palmitic plus stearic acid diet on which the rats lost weight during the month previous of the administration of alloxan. The same protective action was also observed in the rats fed diets high in the ethyl ester of caprylic plus capric acids, a diet on which the animals gained weight. In other words, the protective action occurred whether the animals gained or lost weight. In those cases in which the fat of the diet was an unsaturated

fatty acid, for example, that of the rats fed a high oleic acid diet who gained weight as did those fed a high carbohydrate diet, a marked toxic and diabetogenic action of alloxan was observed. Animals fed diets containing the oils showed growth curves similar to those of animals fed high carbohydrate diets. In this case, the diabetogenic action of alloxan was different and was correlated with the iodine number of the oil used. The administration of vitamin E to the animals had no influence on this difference. Partial hydrogenation of sunflower oil reduced the toxic and diabetogenic action of alloxan.

FREDEEN, Kansas City, Mo.

A HITHERTO UNRECOGNIZED BIO-CHEMICAL DIFFERENCE BETWEEN HUMAN MILK AND COW'S MILK. PAUL GYORGY, Pediatrics **11**:98 (Feb.) 1953.

A specific mutant of Lactobacillus bifidus (var. Penn) isolated from the feces of a breast-fed infant has shown no growth in the usual medium satisfactory for most strains of L. bifidus. It required for its propagation the addition of a specific "growth factor" present in human milk. Cows' milk had only 1/50 to 1/100 of the activity of human milk. The average relative activity was highest for the human colostrum, closely followed by rat colostrum, then by human milk, rat milk, and cows' colostrum (taken on the first day). All the other milks tested, in particular the milk from ruminants such as sheep and goats, in addition to cows' milk, have shown only very low activity. Sows' and mares' milks are slightly more active, guinea pig milk is inactive. This microbiologic growth factor is different from all known vitamins and growth factors. Very slight activity was exhibited by liver compounds and practically none by yeast or meat. Meconium is highly active. Human semen, uterine (cervical) mucus, gastric juice (even in a case of pernicious anemia), saliva, amniotic fluid, and tears are also very active. The growth factor occurs in low and higher molecular form in human milk. In meconium it is present in undialyzable form. Purified blood group Substances A and B are highly active. From human milk, levorotatory active products were obtained containing N-acetyl glucosamine, fucose, and galactose, but no amino acids. N-acetyl glucosamine and N-acetyl galactosamine were only slightly active. Higher activity was exhibited by glucosides of N-acetyl-*d*-glucosamine.

L. bifidus (var. Penn) contains a specific enzyme which inactivates the microbiologic growth factor required by the same strain. The enzymatic inactivation of meconium or purified blood group substance as growth factor is accompanied by reduction of its serologic titer as specific blood group and by the liberation of dialyzable reducing substances, chiefly acetyl-glucosamine.

FROM THE AUTHOR'S SUMMARY.

THE EXCRETION OF SUGARS AFTER THE INTRAVENOUS ADMINISTRATION OF INVERT SUGAR. J. H. P. JONXIS and T. H. J. HUISMAN, Arch. Dis. Childhood **28**:446-449 (Dec.) 1953.

In view of the tendency to reduce diuresis and the rapid utilization of fructose by the cell, invert sugar is more suitable for intravenous administration than dextrose of the same concentration, particularly if the concentration exceeds 5%.

The smaller loss of sugar during administration of invert sugar described by Elman and co-workers is important only if large quantities are given in a relatively short period of time.

KELLY, Milwaukee.

NUTRITIONAL DISORDERS IN CHILDREN WITH SPECIAL REFERENCE TO EDEMA. K. C. CHAUDHURI, Indian J. Pediat. **20**:145-153 (July) 1953.

The author feels that the attention of the profession has been distracted in recent years by the discovery of specific nutrients and their metabolic role from the older nutritional problem of simple caloric inadequacy.

The effect of undernutrition on growth can be devastating. Further, in the early years of life nutritional disturbances can develop to a degree unknown in adult life.

There are three groups of etiologic factors in malnutrition: quantitative, qualitative, and infectious. These may lead insidiously to dystrophy, atrophy, and finally edema. Inadequacy of total calories does not lead to any definite clinical entity except perhaps in the case of protein deficiency. It may or may not be associated with edema.

The multiple changes induced by chronic starvation in childhood are easily recovered by proper attention to dietary balance and caloric intake.

McGUIGAN, Evanston, Ill.

SACCHAROSE-INTOLERANCE IN CHILDREN. PIERRE DELTHIL, Presse méd., Supp. 80, p. 1643 (Dec. 12) 1953.

The use of saccharose, although dating back from 150 years, is now much extended. Saccharose is perfectly tolerated by the great majority of infants. Nevertheless, it may induce disturbances, which, though generally moderate and transient, are worthy of being described. The incidence of saccharose intolerance is, indeed, not infrequent. It occurs in the baby in the first three months of life and is shown by various skin changes or digestive disturbances which contrast with the presence of a good general condition and a normal weight curve. Stool examination may help in the diagnosis, but only the therapeutic test in changing the sugar type affords conclusive evidence by a resulting prompt disappearance of the intolerance disorders. In the child, saccharose dyspepsia is usually caused by excess in sugar consumption. One of its cardinal features is strophulus pruriginosus. Being often unrecognized and mistaken for other conditions, it may induce needless and harmful restrictions in diet.

FROM THE AUTHOR'S SUMMARY.

A NEW CONCEPTION OF THE PATHOGENESIS OF INFANT'S ATROPHY AND THE RESULTING THERAPY. L. KULIN, Ann. pædiat. **181**:320 (Nov.) 1953.

The final cause of atrophy has been recognized as a disparity between anabolism and catabolism. The organism is incapable of assimilation because it is forced to an increased dissimilation. This pathologic state of metabolism is due to a disparity between the weight and the surface of the body in sucklings that is established primarily or by intercurrent diseases. For this reason, the baby is forced to spend a considerable ratio of his total energetic output for compensating loss of heat from the relatively increased surface of the body.

This pathomechanism can be stopped and/or reverted by additional nutrition in exceptional cases only, since the metabolic apparatus of the atrophic organism is lowered in its functional capacity. The increased energy demands cannot be satisfied by additional nutrition. The single way of satisfying these demands is to reduce the amount of heat given off from the surface of the body by warding atrophic sucklings in air-conditioned rooms (82.4 to 91.4 F. [28 to 33 C.] temperature, with a relative humidity of 55 to 70%). By this method the food intake suffices to cause a satisfactory increase of weight by spending the spared energies for assimilation.

FROM THE AUTHOR'S SUMMARY.

A STATISTICAL STUDY OF THE METHODS OF FEEDING BABIES IN THE PROVINCE OF MODENA IN THE FIVE-YEAR PERIOD FROM 1947 TO 1951. S. SANTYAN Y VELASCO, Lattante **24**:3 (Jan.) 1953.

This paper deals with the vital statistics of the province of Modena, and especially of the cases seen in the clinics of the O. N. M. I. The number of babies born in the province in 1947 was 9,309 and had gradually fallen off to 6,914 in 1951. Whereas only 50% of these babies had visited the clinics in 1947, 70% were registered there in 1951. The percentage of the babies being wholly artificially fed has remained about the same throughout the five-year period (22%). The percentage of babies on breast feeding alone has fallen from 52% to 41%, and of those on mixed feedings has risen from 27% to 36%. The number of cases of gastrointestinal and nutritional disease has fallen from 805 (72 deaths) in 1947 to 359 (18 deaths) in 1951.

HIGGINS, Boston.

NOTES ON THE AFTER-CARE AND GROWTH OF DYSTROPHIC INFANTS. B. ANGELINI and E. PENNATI, Lattante **24**:15 (Jan.) 1953.

A center has been established in Milan especially for the follow-up of infants who were dystrophic. Of 1,700 patients in the Pediatric Clinic in 1946, 132 were dystrophic infants. A follow-up of these patients five years later revealed that 12 could not be found, 38 had died, and 12 showed excellent, 54 average, and 18 subnormal growth and development.

HIGGINS, Boston.

INFLUENCE OF PLASMA THERAPY ON BLOOD PROTEIN PICTURE OF DYSTROPHIC INFANTS. M. GOMIRATO-SANDRUCCI and E. TAUBER, Minerva pediat. **5**:963 (Nov. 15) 1953.

Fifteen dystrophic infants between the ages of 1 month and 2 years were given on alternate days injections of 10 to 12 cc. per kilogram of body weight of human plasma to which hyaluronidase had been added. The blood protein picture was determined by electrophoresis before and on the 10th day and in five children again on the 20th day after the injections were begun. The blood of the older babies, whose weight deficit was due to episodes of dyspepsia and irrational feeding, revealed definite increases in total protein and albumin percentages and in the albumin-globulin ratio. In the cases of the younger babies, who were underweight from pyloric stenosis or from failure to adjust to cow's milk feedings, the changes found were not striking and not invariable, although the tendency was toward similar increases.

HIGGINS, Boston.

VITAMIN E IN THE PROPHYLAXIS OF HEMORRHAGE OF THE NEWBORN. PAOLO PROSPERI and SANDRO DELL ORSO, Riv. clin. pediat. **51**:501 (Dec.) 1953.

The authors administered vitamin E by different ways in doses of 500 to 600 mg. to 32 pregnant women in labor pains.

The study on the most hemogenic tests before and after such treatment pointed out a decrease of the coagulation time in 59.3% of the cases, a decrease of the hemorrhagic time in 50%, and a lowering of the time of Howell in 71.8%.

Hemorrhagic manifestations did not appear in any of the newborn infants delivered of mothers who had this treatment; the values of the time of Howell observed from the blood of the umbilical cord of these infants were inferior to the normal in 96.8% of the cases.

After recapitulating the chief theories on the pathogenesis of the "morbus haemorrhagicus neonatorum," the authors consider the action of vitamin E in the prophylaxis of this pathological manifestation.

FROM THE AUTHORS' SUMMARY.

MEDICAL AND SOCIAL PROBLEMS OF MALNUTRITION. FEDERICO GOMEZ, Rev. españ. pediat. **9**:163-179, 1953.

Dr. Gomez writes an excellent paper on the problems of malnutrition in Mexico both from a medical and from a social viewpoint. He distinguishes first between acute and chronic hunger. There is a definite difference between the two. In acute hunger, metabolic rate and all physiological processes are increased in intensity, with the person displaying aggression, anger, and all sorts of efforts to do something about it. This type, if continued, is productive of quick death long before any vitamin deficiencies can develop.

However, except in countries where actual war is being fought, chronic hunger is much more of a problem.

The author takes most of the paper to discuss this type among pregnant women and among children. In chronic hunger, the organism has adapted itself to deficits, and the person appears slow and indifferent. There is fatigue on slight effort, a loss of the sense of responsibility, and no desire to satisfy even the usual ambitions common to all human beings. These mothers are found to have no meat, eggs, or milk in their diet. The children have the same sad anxious facial expressions of their parents. These children show signs of multiple vitamin deficiencies: dry hair and skin, chronic conjunctivitis, glossitis, cheilosis, etc. Although there is scant evidence of pellagra, edema, rickets, and other clinical entities, the cellular nutrition is so poor that intercurrent infections may cause the development of more serious illness. Simple upper respiratory infections or an attack of vomiting or diarrhea may precipitate serious illness. These children also have no resistance to tuberculosis or malaria.

The author divides the syndrome of chronic hunger into three grades according to the weight loss and clinical symptoms. The first may be similar to an acute hunger, as described above.

The causes of malnutrition may be poverty, but much malnutrition is due to ignorance about diet, even among those who are economically able to feed their children well.

ALLEN, Santa Fe, N. Mex.

HUMAN DIET FREE FROM ANIMAL PROTEIN. W. F. DONATH, I. A. FISCHER, H. C. VAN DER MEULEN, VAN EYSBERGEN, and J. F. DE WIJN, Nederl. tijdschr. geneesk. **97**:2118 (Aug. 15) 1953.

A preliminary report from the Dutch Institute for Preventive Medicine (Leyden) of 60 adult vegetarians living one-half to five years without animal proteins. Most of the whole group had macrocytosis without or with slight anemia, carotinemia, comparatively high alkaline phosphatase, and low serum phosphorus. Thirteen out of 100 of the subjects showed deficiency symptoms as angular stomatitis, atrophic tongue, and paradentosis.

VAN CREVELD, Amsterdam.

Vitamins; Avitaminoses

VITAMIN D AND TISSUE CITRATE. H. STEENBOCK and S. A. BELLIN, J. Biol. Chem. **205**:985, 1953.

Experiments were done on rats. It was found that the citrate content of blood, bone, kidney, heart, and small intestine of rats on normal or low-phosphorus rachitogenic diets was increased by physiological doses of vitamin D. Liver citrate was not affected. The authors conclude that the increase in urinary citrate noted by a number of authors as a result of vitamin D administration is a reflection of increased accumulation in certain tissues.

FORBES, Rochester, N. Y.

RICKETS AND ITS INCIDENCE IN MADHYA PRADESH. C. K. GAN, Indian J. Pediat. **20**:218-224 (Sept.) 1953.

The author points out that rickets is not as common as is supposed in his part of India and comments that much so-called rickets is malnutrition. He also states that vitamin D is not the main missing factor of rickets in the tropics.

McGUIGAN, Evanston, Ill.

OBSERVATIONS ON THE USE OF VITAMIN T (GOETSCH) IN PEDIATRICS. S. CUTILLO, Lattante **24**:845 (Nov.) 1953.

Vitamin T, or torulitina, is a preparation made from torulae; Goetsch had observed that insect larvae throve on these yeastlike organisms; the natural assumption was that torulae might have a similar effect on infant growth. In the present study, the vitamin T was given to 2 children with celiac disease, 12 premature infants, and 28 dystrophic infants. The results were very favorable, the patients showing weight gains, increase in the plasma protein content, and rises in the hemoglobin and red cell count of the blood.

HIGGINS, Boston.

CLINICAL AND EXPERIMENTAL STUDIES ON VITAMIN T GOETSCH. G. COTELLESSA and P. SALOMONE, Minerva pediat. **5**:1086 (Dec. 15) 1953.

There was an appreciable and immediate gain in the weights of 28 premature or undernourished infants following the addition of vitamin T (Goetsch) to their feedings.

Experimental observations with rats showed that the vitamin caused a rapid increase in bone growth.

HIGGINS, Boston.

THE ACTION OF LARGE DOSES OF VITAMINE B_{12} GIVEN ORALLY TO BREAST-FED INFANTS WITH A FAT DYSPEPSIA, AND ON THE GROWTH OF HEALTHY NURSING PUPPIES. P. PERITI, Minerva pediat. **6**:30 (Jan. 15) 1954.

The growth of normal breast-fed infants was unaffected when they were given by mouth 50 to 100 γ vitamin B_{12} daily. This same medication, when given to breast-fed babies with a dyspepsia due to fat, resulted in weight gains, more normal stools, and improvement of eczematous lesions.

Normal nursing puppies, after receiving 50 γ of vitamin B_{12} daily for a month, showed no deviation as to weight gain or blood picture from control animals.

HIGGINS, Boston.

A Case of Scurvy. R. Cocchi, Riv. clin. pediat. **51**:379 (Nov.) 1953.

The author describes a case of Barlow's disease observed in a little girl suffering from cerebropathy. After reporting the history of the patient, he analyzes the symptomatology, then the differential diagnosis is outlined.

From the Author's Summary.

D-Vitamin Intoxication in Infancy. J. Jochims, Med. Klin. **49**:546 (April 9) 1954.

A severely ill 4-month-old infant was admitted. A peculiarly pronounced lack of appetite prompted the author to investigate the possibility of a vitamin D intoxication. The infant had been given 3,600,000 units of vitamin D_3 by mouth within 18 days, that is, 90 mg. Originally, it was ordered to prevent rickets, although there was no evidence of it. The most important symptoms are given, such as the characteristic anorexia, which is stressed, vomiting, exsiccosis, infrequent hard stools, cerebral signs, and fever. The calcium of the urine was increased so that the Sulkowitch test was positive. The nonprotein nitrogen of the blood was increased somewhat, and the blood pressure was elevated.

Amberg, Rochester, Minn.

Possible Value of Vitamin B_{12} in the Prevention of Neurotropic Virus Infections (Encephalitis Postvaccinalis, Poliomyelitis). F. J. Keuning, Nederl. tijdschr. geneesk. **97**:284 (Jan. 31) 1953.

Vitamin B_{12} and other liver factors are of great value for the nucleoprotein metabolism in nuclei and cytoplasm. As the virus consists for the greater part of nucleoprotein complex, a correlation is possible between the therapeutic effect of liver extract in the prevention of encephalitis postvaccinalis and the nucleoprotein metabolism in neurotropic virus infections.

van Creveld, Amsterdam.

Hypervitaminosis A. H. J. Klein Obbink and C. Nieman, Nederl. tijdschr. geneesk. **97**:872 (April 4) 1953.

Rats fed daily with 50,000 I. U. of vitamin A acetate show after a week numerous spontaneous fractures, especially of the long bones. In man, acute vitamin A intoxication has been described after eating of the livers of the polar bear, whale, and shark and a chronic form in children and adults after daily intake of a high dose of vitamin A. The latter demonstrate a bone disease resembling infantile cortical hyperostosis (Caffey disease).

van Creveld, Amsterdam.

Hygiene; Growth and Nutrition; Public Health

The Body Size and Form of Present-Day White Elementary School Children Residing in West-Central Oregon. Howard V. Meredith and E. Matilda Meredith, Child Developm. **24**:83 (June) 1953.

White public school children of west-central Oregon are portrayed with reference to 11 measures of body size and 5 measures of body form. The data were collected in 1950-1952 on samples drawn to represent boys 7 and 10 years of age and girls 7, 9, and 11 years of age. Following description of the subjects and specification of the collection procedures, central tendency and variability analyses are presented on each age-sex group for body weight, stature, stem length, and four dimensions each of the trunk and extremities.

A comparative section on body size places in juxtaposition the Oregon children and other groups of white children chosen to approximate state, ethnic, secular, and geographic permutations. Materials are utilized from west-central California, north-central Utah, Minnesota, Texas, Maryland, Virginia, and England.

The aspects of body form fall into two classes, slender-to-stocky continua (length of stem and limbs in relation to girth) and regional-predominance continua (relations between upper trunk and lower trunk). After presentation of central tendency and variability values for form, these original statistics and statistics from the literature are conjoined in the discussion of three topics: age changes in body form, sex differences in body form, and delineation of the body form of individual persons.

From the Authors' Summary.

STANDARD MEASUREMENTS IN FILIPINO INFANTS DURING THE FIRST YEAR. FELIX ESTRADA and ROSALINA CANCIO, Philippine J. Pediat. **2**:1 (April-June) 1953.

A presentation is made of the average measurements of weight and length of normal or apparently normal Filipino infants, mostly born of mothers in the Free Clinics of the Santo Tomas University Hospital, attending the Well Baby Clinic of the Pediatric Department, U. S. T. College of Medicine. Sources of error in the study were pointed out, and comparisons were established with other similar determinations. A phenomenon called the "stoking up" process is mentioned and its discrepancy with the doubling time inferred for purposes of avoiding nutritional errors during the first months. The values obtained compare favorably with the precentile tables of the Harvard School of Public Health.

FROM THE AUTHORS' SUMMARY.

MORBIDITY AND MORTALITY IN A CHILDREN'S MEDICAL UNIT. SISIR K. BOSE, Indian J. Pediat. **20**:209-217 (Sept.) 1953.

A children's unit of 25 beds limited to children of 7 years or younger admitted 900 patients during 1952. Most of these were seriously ill, the unit functioning largely as an emergency ward. Income levels were very low, and the surrounding area was congested, and sanitary possibilities were poor.

Over-all mortality was 35.1%. Infants accounted for 47.1%, 2- to 3-year-olds 32.6%, and 4- to 7-year-olds 20.3%. Nearly half the total deaths occurred within 24 hours of admission.

Respiratory infections were the most common, comprising 16.9% of the total, with a 33.3% mortality. Diarrhea was second, with 12.8% and 47.5% mortality. Tuberculosis, with 6.2% of admissions, enteric fever, with 5.5%, scorpion stings, with 5.4%, and malaria, with 5.3% were the most common diseases. The author stresses the difficulty of coming to any conclusions regarding mortality among urban children from such a study.

McGUIGAN, Evanston, Ill.

Prematurity and Congenital Deformities

THE DEVELOPING FUNDUS OCULI OF THE PREMATURE INFANT AND ITS RELATIONSHIP TO RETROLENTAL FIBROPLASIA. MARY CRITZ FLETCHER, J. Pediat. **43**:499 (Nov.) 1953.

To begin with, Mary Fletcher gives a vivid description of the development of the fundus of the eye from the immature fundus of the very small premature through a transitional stage to the mature fundus of the full-term infant. She says that after maturation has been reached the eye may remain normal or may progress to show early changes of retrolental fibroplasia. These early changes in turn may reverse spontaneously or may progress to the severe stages of the disease with varying degrees of visual impairment.

The smallest infants and those with the most immature fundi at birth are the ones most likely to develop severe retrolental fibroplasia. Small premature infants and those infants with severe retrolental fibroplasia have a high and fluctuating myopia, which may remain as a residual lesion.

The genesis of pathology in retrolental fibroplasia is not yet clear. The author discusses retinal vascular dynamics, oxygen tensions, sex, and race; in her series, white male infants predominated. She concludes that the cause of retrolental fibroplasia is unknown.

MACDONALD, Pittsburgh.

CHONDRODYSTROPHY WITH ECTODERMAL DEFECTS. E. J. GALLAGHER, M. E. MacGREGOR, and M. ISRAELSKI, Arch. Dis. Childhood **28**:18 (Feb.) 1953.

The case is reported of a 12-year-old girl who exhibited ectodermal defects, spinal chondro-osteodystrophy of the Morquio type, and certain other bone and joint deformities.

Resemblances to the Ellis-van Creveld syndrome are discussed.

KELLY, Milwaukee.

BLOOD SUGAR STUDIES ON PREMATURE BABIES. O. CONOR WARD, Arch. Dis. Childhood **28**:194-197 (June) 1953.

The blood sugar has been studied in premature babies in the first two days of life. Low levels have been found, but these were not associated with abnormal symptoms. It is suggested that they are due to a low liver glycogen content, which is depleted by starvation. The endocrine control of the blood sugar in premature babies is discussed.

KELLY, Milwaukee.

THE RESULTS OF A NATIONAL INQUIRY INTO THE GROWTH OF PREMATURE CHILDREN FROM BIRTH TO FOUR YEARS. J. W. B. DOUGLAS and C. MOGFORD, Arch. Dis. Childhood **28**:436-445 (Dec.) 1953.

This paper describes the growth of a national sample of premature children who have been followed up from birth to 4 years of age and who, throughout the period, have been contrasted with a closely matched group of controls.

On the average, the premature children have not reduced their weight handicap between birth and 2 years of age or between 2 and 4 years.

By 4 years of age, 36% of premature children have caught up with or surpassed their controls in weight and 44% in height. There is a tendency for the smallest premature children at birth to be the most successful in eliminating their initial handicaps.

The mothers of premature children are on the average shorter and lighter than the mothers of the controls, and the premature children who are furthest behind their controls in weight or height tend also to be the ones whose mothers are furthest behind the mothers of the controls in these measurements.

The mothers of the premature children who by 4 years of age have eliminated their initial weight or height handicaps are as tall and as heavy as the mothers of the matched controls. In contrast the mothers of the children who are still lagging behind at this age are significantly smaller and lighter than the mothers of the controls.

KELLY, Milwaukee.

THE EXPERIMENTAL PRODUCTION OF CONGENITAL DEFECTS WITH PARTICULAR REFERENCE TO CLEFT PALATE. F. CLARKE FRASER, T. D. FAINSTATE, and H. KALTER, Études néonatal. **2**:43 (June) 1953.

Cortisone injected into pregnant mice produces cleft palate and other defects in the resulting offspring. Compound F does also. The incidence of cleft palate varies with the dose of the drug, the gestational stage at which it is given, and the genetic constitution of the treated animal. Genetic analysis shows that a major part of the difference in resistance of different strains to the teratogenic action of cortisone is due to a genetically determined difference in the mothers, rather than in the embryos. With the appropriate dose, at the appropriate stage, in a genetically susceptible strain of mice, cleft palates can be induced in virtually 100% of the offspring of treated animals, thus providing an opportunity for embryological analysis of the defect. Cortisone can induce cleft palates in offspring of mothers treated at a stage after the embryonic palate is normally closed, suggesting that in some cases cleft palate is the result of a degenerative change, rather than a developmental delay.

FROM THE AUTHORS' SUMMARY.

PRENATAL DISEASES. O. THALHAMMER, Ann pædiat. **181**:257 (Nov.) 1953.

The sphere of antenatal pathology is briefly outlined, and the state of present-day knowledge is intimated. The first step in the exploration of antenatal disturbances is the search for complications in pregnancy which may have an etiological influence. Careful histories were taken in 43 children with congenital disturbances which in 20 cases revealed etiologically suspicious circumstances. The clinical and antenatal histories of these children are shortly described. Conclusive proof for the etiological importance of the "suspicious circumstances" cannot be obtained in the present state of affairs. A questionnaire is produced which should serve as a help when obtaining anamneses, and some experiences are reported which happened when taking down antenatal anamneses.

FROM THE AUTHOR'S SUMMARY.

AN ANALYSIS OF THE CAUSES AND FREQUENCY OF PREMATURITY, ESPECIALLY DURING THE WAR YEARS. M. VERROTTI, Lattante **24**:449 (July) 1953.

Some statistics, covering the years 1936 through 1950, as to prematurity are given, as gathered from the records of the Clinic in Siena, Italy. Of the 10,799 infants, 5.4% born were premature; in the prewar years the percentage was 3.5, in the war years, 5.0, in the early postwar years, 7.3, while in 1950, the percentage had fallen to 5.2. The percentage of premature boys was 54% and of girls 46%; 36% were born before the eighth month of pregnancy, and 55% were born of uniparae. The death rate due to prematurity had not increased during this period.

HIGGINS, Boston.

COMMENTS ON VARIOUS PROCEDURES FOLLOWED IN THE FEEDING OF PREMATURE INFANTS. E. DE TONI, Lattante **24**:458 (July) 1953.

In a discussion of the results of different routines and formulas used in the Premature Center of the University of Genoa Children's Hospital, the author comments that mother's milk, even if modified more or less, is the fundamental basis for assuring a correct and safe diet and for obtaining a constant weight gain.

HIGGINS, Boston.

PROBLEMS OF THE PREMATURE INFANT. JOSE OBES POLLERI, Arch. pediat. Uruguay **24**:487 (Aug.) 1953.

The decisive importance of prematurity lies in its increasing influence upon mortality statistics, where the lowering of the infectious factor tends to leave it each time further from the other causes of death, as the leading cause of infant mortality.

The premature infant's problems can be separated into two main groups, which are in different stages of physiopathological knowledge and effectiveness of pediatric assistance. These are care at birth and later care. As a contribution to the whole report, some of these problems are studied here. The author has experience and personal convictions regarding them.

Fetal Nutritional Deficiency.—Prevention of prematurity and its risks has interesting indications in modern physiopathology which it is necessary to follow: hormonal equilibrium in pregnancy, placental function, uterine conversion, etc. The most promising indication is found in fetal nutrition, where Hammond's doctrine of fetal priorities in the distribution of nutrients of the maternal blood stream, experimentally validated by Wallace and confirmed by modern statistical documentation, offers with the care of maternal diet a simple and secure method for the diminution of the risks of prematurity. Correct feeding during the last quarter of pregnancy must be a fundamental preoccupation of the practitioner and social organization of maternal aid.

Anatomic Clinical Causes of Death.—Careful pathologic studies show concrete causes of the premature infant's death in almost every investigated case, laying aside the old and doubtful label of prematurity; only very small infants (immatures) give a percentage of obscure autopsies. Infection, especially bronchopneumonia, is extraordinarily frequent even in the neonatal period. The hyaline membrane explains many causes of death during the first days. Pulmonary immaturity with immaturity of alveoli and capillary bed is frequent and important in immature infants. Lesions secondary to anoxia are very important. Cerebromeningeal hemorrhage, in the etiology of which anoxia and traumatism are confused, is of classic importance; intraventricular hemorrhage of anoxia is a relatively important cause of death in premature infants of low weight. Pulmonary hemorrhage, though not very frequent, is an interesting finding. Finally, it is necessary to point out the general importance of hemorrhagic pathology which tends to be prevalent in premature infants.

Feeding.—The premature infant that does not have an increase in weight runs the risk of dying. Human milk duly complemented is the selected food. Protein complements will preferably be obtained with amino acids, but also with calcium caseinate, buttermilk, etc. Artificial food allows one to obtain very good results within a strict technique, but human milk is received with a greater tolerance and is more successful. Tolerance should be sought during the first days. Subsequently, the value of the diet will be raised according to tolerance, demand, and evolution of weight. Vitamins are very important. Hospital methodical arrangement is a fundamental factor in success, and efficient nursing is especially decisive.

Treatment of Infection.—Infection dominates the premature infant's pathology; the important decrease in premature mortality is caused by its treatment with modern anti-infectious agents. Prophylaxis rests on aseptic technique, modern architecture and material, correct organization, and, especially, a trained staff in sufficient number. In practice, these factors are lacking and the use as preventives of proper antibiotics, in spite of their real risk, is necessary. Anti-infectious treatment must be intensive and start early, even so far as to be confused with prophylactic treatment in practice, because of the characteristics of the premature infant's infection, which is serious, inapparent, and rapidly advancing. Choice of the anti-infectious agent and its possible association depends on the probable micro-organism and on the antimicrobian spectra. The marvelous group of anti-infectious agents of the present time, such as sulfadiazine, penicillin, streptomycin, chlortetracycline, chloramphenicol, oxytetracycline, and erythromycin, has extraordinarily widened the practical possibilities of treatment. Dosage and schedule follow the classic rules. The possibility of lengthening the interval between doses in terms of the lesser renal permeability in the premature infant during the first weeks must be considered. The duration of the treatment must be from five to seven days as a minimum, and the substitution of one agent for another must be made early, within 24 to 48 hours.

Premature Infant's Blood Transfusion.—Transfusion of blood, plasma, and red blood cells is a very valuable element in the premature infant's treatment and support. In practice, difficulties do not exist and risks are very limited if correct technique is used, and to be disregarded if we compare them with the possible benefit.

In birth crisis, blood transfusion is useful in cases of shock and dehydration, in edema, and in increase of carbonic anhydrase or its activity. It is also useful as a support of premature infants who have difficulty in their progress to maturity in the later stages. In early anemia it is essential as a substitute for the lack of reaction in premature infants and later on as a relief of the correspondent mechanism. It is a classic part of the treatment of systemic reaction in infant diarrhea. It is very important in the complex hemorrhagic syndrome. In atrophy, massive blood transfusion repeated, as a compensation for latent shock and to supply protein, has decisive value in gaining time and correcting the so far irreversible picture of "decomposition" while digestive tolerance is restored.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON THE GASTROINTESTINAL TRACT OF PREMATURE INFANTS. V. DIETEL and R. SCHMOEGER, Monatsschr. Kinderh. **101**:433 (Oct.) 1953.

By means of x-ray opaque contrast media, it was demonstrated that in premature infants human breast milk given by bottle remained in the stomach 30 minutes longer than when given by gavage. The milk did not always enter the duodenum immediately thereafter. In the upright position, gastric retention was shorter than in the recumbent. Decreasing the quantity of milk by one-half did not reduce its length of gastric retention correspondingly. Cold milk administered by gavage passed through the stomach and small intestine more slowly than when it was warmed. Passage throught the small intestine in premature infants was slower than in full-term infants. After six hours, milk had usually progressed into the cecum in full-term infants but had not reached it in 13% of premature infants. Passage through the entire gastrointestinal tract took 16 hours. Gavage-fed milk remained in the large intestine a shorter time than bottle-fed milk.

HARTENSTEIN, Syracuse, N. Y.

CAUSES OF RETROLENTAL FIBROPLASIA. P. J. WAARDENBURG, Nederl. tijdschr. geneesk. **97**:814 (March 28) 1953.

A survey is given of cases of retrolental dysplasia in twins observed in the Netherlands and abroad. It seems probable that anoxia is an important etiological factor; the question whether a hereditary or nonhereditary disposition exists also remains undecided. The problem can only be approached on the basis of a comparative study of monozygotic and dizygotic twins, which study presumes a distinct diagnosis of the twin groups. This is not mentioned in the literature of the past 10 years. The reliable data collected thus far do not afford arguments in favor of a hereditary disposition.

VAN CREVELD, Amsterdam.

Newborn

STUDIES OF THE IMMUNOLOGY OF THE NEWBORN INFANT: IV. ANTIBODY FORMATION IN THE PREMATURE INFANT. JOSEPN DANCIS, JOHN J. OSBORN, and HANS W. KUNZ, Pediatrics **12**:151 (Aug.) 1953.

The antibody response of premature infants immunized at birth with a single injection of diphtheria toxoid was compared to that of a group of term infants similarly immunized. No significant difference was demonstrated.

A group of premature infants was immunized at about the time that was estimated to be their normal birth date and the antibody response compared to that of term infants at birth. The performance of the premature infants was superior to that of the term infants.

The significance of these findings is discussed.

FROM THE AUTHORS' SUMMARY.

VESTIBULAR RESPONSE TO ROTATION IN THE NEWBORN INFANT. MARGARET M. LAWRENCE and CARL R. FIEND, Pediatrics **12**:300 (Sept.) 1953.

Using a newly designed rotating apparatus with control of acceleration, deceleration, and speed, the response of 63 full-term newborn infants to rotation was studied.

While awake, all infants showed head and eye deviation opposite to the direction of rotation during acceleration and in the same direction during deceleration; all infants had a normal nystagmus during acceleration and for several turns of constant speed. Then followed a reversal of the the nystagmus as soon as deceleration took place. The duration of postrotational nystagmus following 10 turns in 20 seconds varied from 3 to 35 seconds, with an average of 13.1 seconds. There is no comparable adult group reported, as the stimulus is not constant or controlled.

Sleeping infants had no response to rotation even though they have normal responses while awake.

Associated postrotation reactions were flushing, eructation, and voiding.

The literature on vestibular responses to rotation in the newborn infant has been reviewed.

FROM THE AUTHORS' SUMMARY.

STUDIES OF THE IMMUNOLOGY OF THE NEWBORN INFANT: V. EFFECT OF DIETARY PROTEIN ON ANTIBODY PRODUCTION. JOSEPH DANCIS, JOHN J. OSBORN, and JUAN F. JULIA, Pediatrics **12**:395 (Oct.) 1953.

Two groups of 10 infants each were maintained on isocaloric milk formula in which the protein content differed. One group received a milk formula containing 2.0% protein, providing approximately 3 gm. protein per kilogram of body weight, and the other group received a formula containing 3.6% protein, providing approximately 5½ gm. per kilogram of body weight. Both groups were immunized with diphtheria toxoid and the antitoxin response measured.

No difference in the antitoxin response between the two groups was seen.

This suggests that a high level of milk protein in the diet does not measurably improve the ability to produce antibodies.

FROM THE AUTHORS' SUMMARY.

CONGENITAL TOXOPLASMOSIS IN THE NEWBORN. E. G. HALL, J. D. HAY, P. D. MOSS, and M. P. RYAN, Arch. Dis. Childhood **28**:117-124 (April) 1953.

The clinical, morbid anatomical, and histological details of two cases of congenital toxoplasmosis presenting somewhat unusual features at birth are described. Toxoplasma were identified in both cases. The significance of some of the extraneural lesions is discussed and the absence of specific changes in the placentas noted.

KELLY, Milwaukee.

BLOOD GLUCOSE CHANGES IN THE NEWBORN. R. D. G. CREERY and T. J. PARKINSON, Arch. Dis. Childhood **28**:134-139 (April) 1953.

Previous work on the blood-glucose level of newborn babies is reviewed briefly and the absence of intensive serial study noted.

Results are presented to show the changes which took place in 46 normal babies born spontaneously to normal unanesthetized mothers.

It was found that during the first hour after delivery, the babies' blood glucose fell from 79 mg. per 100 ml., as found in the umbilical vein, to a mean value of 52 mg. per 100 ml. and that this level was maintained with varying constancy in individual babies.

From a total of 356 estimations, it is concluded that the normal blood-glucose range for babies between 1 and 12 hours old is 30 to 75 mg. per 100 ml.

This range appears to narrow slightly but progressively during this period.

There is no difference in blood glucose between baby boys and baby girls.

There is no relationship between the birth weight of these full-term babies and the mean of the blood glucose at 3, 6, 9, and 12 hours.

KELLY, Milwaukee.

ACUTE ISOLATED MYOCARDITIS IN NEWBORN INFANTS. J. M. DRENNAN, Arch. Dis. Childhood **28**:288-290 (Aug.) 1953.

Two fatal cases of acute isolated myocarditis occurring in newborn infants are described.

The lesions in the myocardium were focal in distribution and showed a peculiar degenerative change limited to the sarcoplasm of the affected muscle fibers.

The relationship of this parenchymatous lesion to the commoner interstitial type is discussed.

There was no response to treatment with various antibiotic agents.

KELLY, Milwaukee.

URTICARIA NEONATORUM (ERYTHEMA TOXICUM NEONATORUM). H. V. L. FINLAY and J. P. BOUND, Arch. Dis. Childhood **28**:404-408 (Oct.) 1953.

A clinical description of the urticaria seen in the neonatal period, the so-called erythema toxicum neonatorum, is given and a short reference to the previous literature is included.

The rash is found in two forms: (1) a simple type, and (2) a pustular type.

Observations are made on a series seen in a maternity unit, which included 25 cases of the pustular type. The lesions in the pustular type are shown to be due to a massive local outpouring of eosinophile leucocytes. The resemblance of the pustular type of urticaria neonatorum to staphylococcal pyodermia is stressed, and a smear method of rapid diagnosis recommended for doubtful cases.

Occasionally the pustular type becomes secondarily infected.

Uninfected urticaria neonatorum requires no treatment.

KELLY, Milwaukee.

INVOLUTION OF THE LEFT LIVER IN THE NEWBORN AND ITS RELATIONSHIP TO PHYSIOLOGICAL ICTERUS. JOHN L. EMERY, Arch. Dis. Childhood **28**:463-465 (Dec.) 1953.

There is a rapid involution of the left lobe of the liver beginning just after birth and completed within four or five days of birth.

This involution seems to be the direct result of changes in blood supply to the liver associated with birth.

The involution of the left liver coincides with the known period of deficient functional activity of the liver in the newborn. It is probably the cause of the temporary hepatic inadequacy during the first few days of life, hence the cause of the postnatal rise in bilirubin level associated with physiological icterus.

KELLY, Milwaukee.

THE PATTERN OF HAEMOLYTIC DISEASE OF THE NEWBORN. BARBARA S. DAVIES, JOHN GERRARD, and J. A. H. WATERHOUSE, Arch. Dis. Childhood **28**:466-470 (Dec.) 1953.

Families with babies having hemolytic disease of the newborn have been classified into two main groups depending on the gravity of the disease in the first affected baby. If this first affected baby has a mild form of the disease, i. e., is not hydropic or stillborn, then in 83% of cases the next affected will also be a mild case. If this first affected baby is hydropic or stillborn, then in 80% of cases the next affected will also be hydropic or stillborn, if delivered at term.

Women whose first affected baby is hydropic or stillborn have three times as many subsequent pregnancies as do those whose first affected is a mild case; the women who are least likely to have a viable infant endeavor most to obtain one. If such women are allowed to go into labor spontaneously, the baby will usually be stillborn or hydropic; it is suggested that, unless the husband is heterozygous, in these cases the premature induction of labor is indicated.

By contrast, women whose first affected baby is a mild case need not necessarily be discouraged from having another infant, because affected children born subsequently are usually mild cases also.

KELLY, Milwaukee.

PNEUMOPATHY OF THE FETUS AND NEWBORN. ROBERT CLEMENT, Presse méd. **61**:149 (Feb. 7) 1953.

In 20% of deadborn and 25% of infants dead shortly after birth there are pulmonary lesions; these seem responsible for 4 to 5% of deaths occurring within the early 12 days of life.

The lesions are often mere anatomic findings which may give rise only to undefined symptomatology and are radiologically interpreted with difficulty.

Although all types of inflammation in bronchioles and alveoli were observed, there were some characteristics of congenital pneumopathy, such as profuse proliferation and desquamation of the bronchial epithelium, interstitial infiltration, and presence of mononuclear cells with cytoplasmic inclusions.

Sucking up of sterile amniotic water is at times responsible for asphyxia; it may be an indirect cause of bronchopneumonia, but this is experimentally achieved only when the amniotic water was septic. Asphyxia is not caused by the water but by the solid or viscid particles that obstruct alveoli and bronchi.

Bronchopneumonia in the first days of life is exceptionally due to organisms from the mother's genital tract but most often to contamination through the air tract or to penetration of food particles into the respiratory passage.

The development of a "hyalin-like" membrane which accompanies certain atelectases in the newborn and seems responsible for the death of the latter is caused by the stay in an atmosphere either too rich in oxygen or too dry and may be favored by the sucking up of the amniotic water.

FROM THE AUTHOR'S SUMMARY.

CHANGES IN THE HEMOGLOBIN OF THE NEWBORN FROM RHESUS ANTIBODIES. F. HATZ and E. BERGER, Ann. pædiat. **180**:22 (Jan.) 1953.

The authors report on experiments which show that the alkali resistance of hemoglobin of newborn children is reduced if a serum with a high titer of Rhesus antibodies is acting on Rhesus-positive blood. The results show further that the antigen-antibody reaction which takes place in the erythrocytes does not only manifest itself in the characteristic appearance of agglutination and hemolysis. The alteration of the hemoglobin, as evidenced by the decreased alkali resistance, could always be demonstrated by our experimental methods, while hemolysis was not constantly present.

FROM THE AUTHOR'S SUMMARY.

THE CRITICAL PERIOD OF ADAPTION BY THE NEWBORN INFANT; THE ELIMINATION OF URIC ACID, CREATININE AND 17-KETOSTEROIDS IN THE NEONATAL PERIOD. M. VERROTTI, Clin. pediat. **35**:16 (Jan.) 1953.

Curves were plotted of the daily urinary excretion of uric acid, creatinine, and 17-ketosteroids during the first nine days of life of 10 newborn infants.

Uric acid was excreted in very large amounts during the first four days; this would appear to indicate a high level of nucleoprotein catabolism; there may be uric acid renal infarcts formed.

There was found to be a fairly constant level of creatinine excretion during the neonatal period, indicating a normal creatinine metabolism from birth.

During the first few days of life 17-ketosteroids are excreted in abundant amounts; thereafter, there is a period when practically none are excreted.

These findings represent but a part of the humeral and metabolic changes to which a newborn infant must adapt. The newborn infant's adrenal cortex and pituitary gland must be physiologically active in order to meet this period of crisis.

HIGGINS, Boston.

HISTOCHEMICAL CHANGES IN THE MAMMARY GLANDS OF THE NEWBORN INFANT. B. RONDININI, Clin. pediat. **35**:924 (Dec.) 1953.

Mammary gland tissue from 12 newborn infants was examined by histochemical methods. There were histological changes similar to those found in the functioning adult gland in 6 of the 12 infants; stains in these cases also revealed that the ducts contained drops of fat, mostly neutral lipids. Two premature infants did not show these changes, but two of a set of triplets did.

HIGGINS, Boston.

SUPPURATIVE PAROTITIS IN THE NEWBORN. M. POZZAN, Lattante **24**:818 (Oct.) 1953.

Two infants developed parotitis shortly after birth; purulent material, expressed from Stensen's duct, in one case yielded a culture Staphylococus albus, and in the other case Staphylococcus aureus and Neisseria catarrhalis. Speedy recovery followed antibiotic therapy, penicillin in the first and penicillin and streptomycin in the second case.

HIGGINS, Boston.

AGGLUTINATION CURVES FOR ANTIBODIES A AND B IN THE NEWBORN. ANDRES GONZALES-MENESES PARDO, Acta pediat. españ. **11**:151-175 (Feb.) 1953.

The author studied the agglutination of Group A and Group B antibodies in 40 newborn infants. The mothers were divided into five groups as follows: AA, BB, OO, AO, and OA.

None of the mothers examined in this group of 40 had the groupings BO, OB, AB, or BA.

The infants were studied from birth and some were followed for as long as 15 months with serum agglutination studies.

The children born to the five groups of mothers fell into seven groups. The details of the technique and numerous graphs are included. The conclusions based on this study are as follows:

1. The majority of infants carry in their red cells the agglutinogen characteristics of a well-differentiated group, which remains invariable.

2. A minority presented immature red cells lacking in agglutinogens and in agglutinins in their serum.

3. The majority of newborn, in this group, one-third, lacked agglutinins anti-A and anti-B in their serum.

4. A minority of children carried at birth agglutinins which coincided with those of the mother. These agglutinins disappeared by gradual diminution in variable lengths of time. The time varied from 3 to 15 days after birth.

5. These disappearing agglutinins are believed to be from the maternal blood and not elaborated by the child.

6. It appears that the infant does not have the capacity to form antigroupal agglutinins until he is between 5 and 7 months of age.

7. There seems to be a parallelism between the behavior of these agglutinins and immunity to certain infections, especially measles, in the first few months of life.

ALLEN, Santa Fe, N. Mex.

NUTRITION OF THE NEWBORN IN THE LIGHT OF NEW NUTRITIONAL INVESTIGATIONS. ERICH ROMINGER, Med. Klin. **48**:261 (Feb. 27) 1953.

Natural feeding is to be preferred whenever possible during the first days; even 12 hours after birth an addition of 30 to 40 ml. of water and 3 gm. of sugar per kilogram of body weight is permissable. A mixture of glucose and fructose is better than glucose. When sufficient breast milk is available, usually by the fifth day, the addition of the sugar water is to be omitted. In no case, whether breast-fed or artificially fed, should the infant be permitted to go without sufficient food after 10 days. In case of artificial feeding, a mixture of canned buttermilk with 8 to 10% sugar is recommended. Reasons are given why only a few corrections of the classic nutritional regimen have a scientific foundation.

AMBERG, Rochester, Minn.

DIAGNOSIS AND THERAPY OF ATELECTASIS IN THE NEWBORN. L. VAN DER HAL, Nederl. tijdschr. geneesk. **97**:7 (Jan. 3) 1953.

Good results are obtained in the treatment of atelectasis in the newborn and some prematures by inhalation of a mixture of penicillin, glycerin, and hyaluronidase, combined with intramuscular penicillin. It is assumed that glycerin exsiccates the bronchial secretions by its hygroscopic action; this makes expectoration easier.

VAN CREVELD, Amsterdam.

Acute Contagious Diseases

THERAPEUTIC DOSES OF GAMMA GLOBULIN IN THE TREATMENT OF MEASLES ENCEPHALITIS AND ENCEPHALOMYELITIS. L. ODESSKY, A. V. BEDO, K. G. JENNINGS, I. J. SANDS, P. ROSENBLATT, H. WEISLER, and B. NEWMAN, J. Pediat. **43**:536 (Nov.) 1953.

This is a report of 41 cases of measles, encephalitis, and encephalomyelitis. The authors suggest that gamma globulin in a dose of 1 cc. per pound (0.5 kg.) of body weight given intramuscularly in divided doses over a 36- to 48-hour period as soon as signs and symptoms of central nervous system involvement appear hastens recovery and reduces sequelae. Adjunctive therapy is mandatory, they say, to assure the fullest recovery.

There were no local or systemic reactions to the therapeutic doses of gamma globulin.

The authors suggest that gamma globulin and adjunctive therapy can be used in the treatment of viral complications of the central nervous system other than measles with good results.

MACDONALD, Pittsburgh.

FATAL GENERALIZED VACINIA WITH FAILURE OF ANTIBODY PRODUCTION AND ABSENCE OF SERUM GAMMA GLOBULIN. S. E. KEIDAN, K. MCCARTHY, and J. C. HAWORTH, Arch. Dis. Childhood **28**:110-116 (April) 1953.

A fatal case of generalized vaccinia in a baby is described. Secondary lesions developed two weeks after vaccination, and fresh lesions continued to appear until death occurred, five weeks later.

No neutralizing antibodies for vaccinia virus could be demonstrated in the child's serum, and electrophoretic analysis showed complete absence of gamma globulin.

KELLY, Milwaukee.

FOETAL VACCINIA. A. M. MACDONALD and P. MACARTHUR, Arch. Dis. Childhood **28**:311-314 (Aug.) 1953.

A description is given of the clinical and pathological findings in a premature infant born three months after the primary vaccination of the mother. It is claimed that the child was infected with the virus of vaccinia in utero and was born suffering from generalized congenital vaccinia. Previous reports of a similar condition were sought, and only one other example of the disease has been found.

The pathogenesis of the condition is discussed in the light of the present case, and the rarity of this complication of vaccination is emphasized.

KELLY, Milwaukee.

AN INVESTIGATION INTO CERTAIN ASPECTS OF PERTUSSIS. C. W. KESSON and MARIANNE HARLING, Arch. Dis. Childhood **28**:409-411 (Oct.) 1953.

A review of 224 cases of pertussis showed that lung complications occurred in 28 (12.5%). The sole complication detected was pulmonary collapse.

In most children with pulmonary collapse, following this infection lung reexpansion was spontaneous and complete, usually within two months.

A chest x-ray should be taken in all young children about two to three months after pertussis.

Prevention of contact with a sufferer is not often a practical proposition and will not cause any appreciable decrease in the number of those infected or raise the age incidence of the disease. Safe and efficient vaccination seems to be the only solution.

The incidence of pertussis in children exposed to the infection in their own homes was 76.3%.

Pertussis does not appear to favor the development of tuberculosis.

KELLY, Milwaukee.

STUDIES ON A LONG RANGE ASSOCIATION BETWEEN BULBAR POLIOMYELITIS AND PREVIOUS TONSILLECTOMY. R. V. SOUTHCOTT, M. J. Australia **2**:281-298 (Aug. 22) 1953.

Previous studies had shown that 90% of patients with bulbar poliomyelitis had had previous tonsillectomies, only one of these recently. In order to explore further this relationship, 9,000 school children were surveyed.

Studies showed that the tonsillectomized group was predisposed to bulbar poliomyelitis. This predisposition was shown in the 17-year and older age group, indicating a long duration of the effect of tonsillectomy. The association between tonsillectomy and bulbar poliomyelitis indicates a probable pharyngeal port of entry of the virus.

McGUIGAN, Evanston, Ill.

INCIDENCE OF CONGENITAL MALFORMATIONS FOLLOWING MATERNAL RUBELA AT VARIOUS STAGES OF PREGNANCY. L. S. COLLINS, M. J. Australia **2**:456-458 (Sept. 19) 1953.

Studies of pregnancies complicated by rubella indicated very high percentages of affected infants in the first four months, with sharply lower figures after that period. Percentages in the first four months were, respectively, 79, 90, 80, and 78%. Succeeding months averaged about 24.5%. Three hundred eighty-three pregnancies were investigated.

McGUIGAN, Evanston, Ill.

SIMULTANEOUS IMMUNIZATION OF INFANTS AGAINST WHOOPING-COUGH, DIPHTHERIA AND TETANUS. E. A. NORTH, J. J. LEHMANN, and R. W. PATTERSON, M. J. Australia **2**:740-745 (Nov. 14) 1953.

Conflicting reports regarding combined antigens in young babies are discussed. The authors conclude that the procedure is of value if "booster" injections are given in 6 to 12 months after the original course.

McGUIGAN, Evanston, Ill.

THE COMPARATIVE RESULTS IN CASES OF SCARLET FEVER OF TREATMENT WITH AND WITHOUT PENICILLIN. A. PAPALE and A. KONECNY, Gior. mal. infett. e parassit. **5**:348 (Sept.) 1953.

Statistics are presented as to 1,696 cases of scarlet fever treated in the Ospedale Maria Maddalena in Trieste, from 1947 through 1952. Some of the patients received penicillin in the initial phases of the disease, some at the appearance of complications, and others received no penicillin at all. Penicillin did not seem to exercise any strikingly favorable effects on the duration of the initial febrile period or lessen the number of complications; it did, however, attenuate the severe and toxic symptoms of the disease and lessen the severity of the complications.

HIGGINS, Boston.

CLINICAL AND IMMUNOBIOLOGICAL EXPERIENCE OBTAINED IN PERTUSSIS IMMUNIZATION: PRACTICAL VALUE AND CONTRAINDICATIONS. ANTONIO MONTERO RODRIGUEZ, Acta pediat. españ. **11**:60 (Jan.) 1953.

In a very complete manner, Dr. Rodriguez reviews the literature regarding immunization against pertussis.

Justification for immunization is summed up in the following reasons: (1) diminution of the number of cases, (2) diminution of complications, (3) the immunization is innocuous to most children, and (4) the death rate is lowered, especially in children under 2 years of age.

The investigators of the use of a vaccine for prevention of whooping cough are named and their contributions cited. Thirty-four different men working in various countries and their findings in the study of pertussis are cited.

The largest number of cases occur under 5 years of age and the highest mortality under 2 years of age.

The complications are described and are much more serious than ordinarily realized. Among the series cited by Knopfelmacher, secondary infection with tuberculosis followed in over 4% of children suffering from untreated pertussis.

Hydrocephalus and other neuropathies are not quite as common but are in high enough percentage to be noted.

Common complications of less grave import are bronchiectasis, empyema, and pleuritis.

The next section of this paper is devoted to the various methods of preparing vaccines and the detailed dosage worked out by the 34 investigators.

The age at which the antibodies are most quickly elaborated and some of the immunological data are given. The advantages and disadvantages of giving pertussis vaccine to pregnant women at the sixth month of pregnancy are given. The use of the triple-antigen injection, protecting against diphtheria, tetanus, and pertussis, is very popular in many countries.

Other subjects discussed are the value of immunization from the public health standpoint, cutaneous testing, criticisms and contraindications, and obligatory immunization. The author favors obligatory immunization.

ALLEN, Santa Fe, N. Mex.

ACUTE BRONCHIAL DILATION DUE TO PERTUSSIS. R. A. MARQUEZY, Rev. españ. pediat. **9**:611 (May-June) 1953.

The author feels that a lipoid study of the bronchial tree will enable the physician to distinguish between simple purulent bronchitis following pertussis and permanent chronic bronchial dilatation. The former is acute and subject to treatment. The author discusses his experience in this line of work. Several roentgenograms are included in the article.

ALLEN, Santa Fe, N. Mex.

MODERN CONCEPTS OF THE PATHOGENESIS AND COURSE OF THE DISEASE OF HEINE-MEDIN. J. D. VERLINDE, Nederl. tijdschr. geneesk. **97**:929 (April 11) 1953.

The preparalytic symptoms of the disease of Heine-Medin have to be considered as a specific part of the illness. These are often the only symptoms of the disease. The neural spread of the virus is preceded by a viremia via the muscles, except in cases of bulbar paralysis following tonsillectomy. The paralytic form of the disease of Heine-Medin after inoculation or physical strain can be explained in such a way that the affected muscles invaded by the virus give an easier pathway to secondary neural transportation of the virus than normal muscle tissue.

VAN CREVELD, Amsterdam.

THE ORTHOPEDIC TREATMENT OF ACUTE ANTERIOR POLIOMYELITIS. C. SCHAAP, Nederl. tijdschr. geneesk. **97**:936 (April 11) 1953.

In the treatment of poliomyelitis, application of a plaster cast to the affected extremities is recommended. A thick layer of cotton on the inside of the cast does not inhibit the normal physiological stimuli and muscle contractions. Early mobilization is possible and necessary.

VAN CREVELD, Amsterdam.

Acute Infectious Diseases

NONSPECIFIC MYOCARDITIS IN ACUTE RHEUMATIC FEVER. O. SAPHIR and R. LANGENDORF, Am. Heart J. **46**:432 (Sept.) 1953.

Postmortem studies were carried out on 22 patients who died of acute rheumatic heart disease. All hearts were enlarged. Acute endocarditis involving one or more valves was found in every instance. Recent or old pericarditis was present in 17.

Microscopic study revealed Aschoff bodies in every heart. In addition, nonspecific interstitial myocarditis was encountered in every instance. In 18 hearts, parenchymatous changes occurred

consisting of circumscribed minute foci of degenerated or necrotic muscle fibers surrounded by endothelial leucocytes and lymphocytes, with an occasional mast cell, thus resembling granulomas.

The authors believe that the changes involving the muscle fibers themselves are of much greater importance in regard to the functions of the heart than either Aschoff bodies or interstitial inflammation.

GIBSON, Chicago.

STREPTOCOCCUS IN THE ETIOLOGY OF DIVERSE DISEASES INCLUDING DISEASES OF THE NERVOUS SYSTEM. EDWARD C. ROSENAU, J. Nerv. & Ment. Dis. **117**:415 (May) 1953.

This is a review of the concepts of focal infection in general and of the work done over the years by Rosenau in the field of specificity of streptococcal activity. The paper does not lend itself to abstracting.

JAHR, Omaha, Neb.

BRUCELLOSIS IN AN ESKIMO BOY. M. MATAS and C. CORRIGAN, Canadian M. A. J. **68**:531 (Nov.) 1953.

An Eskimo boy who had never been out of the Arctic except for a year spent in a large tuberculosis sanitarium, was found to have Brucellosis, with proved culture of the bone marrow. While in the sanitarium, he had received large doses of streptomycin. No source of the infection is known, and his was the first positive culture in 10 years in the province of Alberta.

McGUIGAN, Evanston, Ill.

TYPHOID OSTEITIS IN INFANCY. HARRIS JACKSON, I. KESSEL, S. N. JAVETT, and P. KUSHLICK, Arch. Dis. Childhood **28**:23 (Feb.) 1953.

Two cases of typhoid bone lesions in the first year of life are reported. The metaphysis of the upper end of the humerus was affected in both cases. In one case the lesion was bilateral, in the other unilateral. One case also developed bilateral osteochondritis, osteitis, or hyperaemic deossification of the epiphyses, with subsequent reformation and slight deformity. The other case, diagnosed earlier, showed complete return to normal. Chloramphenicol therapy was used in both cases. The literature is briefly reviewed.

KELLY, Milwaukee.

A PLEA FOR IMMUNIZATION OF CHILDREN IN INDIA WITH COMBINED DIPHTHERIA AND TETANUS TOXOIDS. D. C. LAHIRI, J. Indian M. A. **23**:45 (Nov.) 1953.

Diphtheria is widespread in India, with a mortality of 20 to 25%. Tetanus also causes a high mortality, with 300 deaths in children every year in Bombay alone. Because of these figures, it is felt that combined immunization with diphtheria and tetanus toxoids is an urgent need in India and one which could be carried out at comparatively low cost.

McGUIGAN, Evanston, Ill.

RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE IN EGYPT. M. RAHMAN, M. IBRAHIN, A. SOROUR, A. EL-SHERIF, and L. EL RAMLY, J. Egyptian M. A. **36**:611-622, 1953.

A rather general discussion of rheumatic fever is presented. Figures relating to incidence in Egypt especially are not presented.

McGUIGAN, Evanston, Ill.

CLINICAL CHARACTERISTICS OF VIRUS INFECTIONS IN INFANCY. CARLOS VASQUEZ GONZALES, Acta pediat. españ. **11**:198-232 (Feb.) 1953.

The author divides his study into (1) the general characteristics of the virus as a pathogen, (2) the size and modes of culture, (3) isolation, and (4) diagnostic procedures. The affinity of most viruses for a specific tissue is discussed and the development of immunity.

The viruses classified as generalized include yellow fever dengue, pappataci fever, infectious mononucleosis, and acute infectious lymphocytosis.

The dermatotropic category includes the largest number. Each entity is briefly outlined as to clinical diagnosis and treatment. Many of these are selflimited infections not affected in the course of illness by antibiotics.

In discussing the neurotropic viruses, the two classifications include those affecting only the nervous system and those affecting other tissues also. In the former are poliomyelitis and rabies. In the second group there are those which affect the nervous system predominantly, such as the various forms of epidemic encephalitides. Various acute infections of viral nature may also cause nervous involvement occasionally, such as the encephalitides following parotitis, herpes, and measles.

There are also conditions of obscure origin which may be due to a viral infection, such as encephalomyelitis disseminata neuronitis and postinfectious encephalitis. Neuronitis or the Guillain-Barré syndrome is relatively frequent in the first year of life.

The virus diseases of the respiratory and digestive systems are very frequent in children. Primary atypical pneumonitis and hepatitis and viral diarrhea are discussed at length.

The ocular virus diseases include inclusion conjunctivitis and epidemic keratoconjunctivitis. The author based his remarks on his pediatric service at Madrid hospitals and rarely distinguishes between the various infections he has seen and the information gleaned from other sources.

ALLEN, Santa Fe, N. Mex.

TREATMENT OF RHEUMATISM IN CHILDREN WITH IRGAPYRIN. T. HOCKERTS, Deutsche med. Wchnschr. **78**:669 (May 1) 1953.

Irgapyrin, a mixture of Pyramidon and Butazolidin is recommended for treatment of acute polyarthritis. It is given intramuscularly in doses of 3 to not more than 4 ml. daily on six consecutive days. This may be repeated after an interval of not less than six to eight days. Exceptionally, as many as 36 injections were given. Swelling and pain of joints recede rapidly, fever and sedimentation rate of the red blood corpuscles recede after three to four days, at the earliest. Forty patients were treated with Irgapyrin, 16 of these on first admission with acute polyarthritis. In none of these did a cardiac involvement occur, in spite of recurrences. To avoid recurrences, a combination with penicillin therapy is recommended. No evidence of bone marrow lesion was observed, but in three cases a hepatocellular icterus occurred which healed promptly. A microhematuria and exanthemas may occur.

AMBERG, Rochester, Minn.

Chronic Infectious Diseases

CARDIAC INVOLVEMENT IN MILIARY TUBERCULOSIS. TSENG, HSIANG-LEU, and F. ROULET, Am. Rev. Tuberc. **68**:771 (Nov.) 1953.

Tuberculous myocarditis and tubercles of the heart muscle are rarely found at postmortem examination. These findings, plus the even more unusual involvement of the coronary vessels, were present in a 30-year-old woman who died with signs of respiratory failure. Detailed macroscopic and microscopic studies are presented.

ROYCE, Pasadena, Calif.

THE INTERPRETATION OF TESTS FOR TOXOPLASMOSIS. I. A. B. CATHIE and J. A. DUDGEON, Great Ormond St. J. **5**:13-18 (June) 1953.

Intradermal toxoplasmin is a reliable diagnostic test. Dye tests and cytoplasm-modifying antibody tests are also useful, as are complement fixation tests. The authors feel that for any diagnosis of acute or chronic toxoplasmosis the complement-fixation test should be positive. Positive dye tests do not always indicate active infection, since the dye does not disappear with the end of infection, as does the complement fixation. Intradermal tests also remain positive, so that while infection can be demonstrated by either the dye test or the intradermal test, the complement fixation must be done to determine presence of active infection.

McGUIGAN, Evanston, Ill.

SOURCE OF TUBERCULOUS INFECTION IN PATIENTS OF THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN. R. M. MILLS, M. J. Australia **2**:374-376 (Sept. 5) 1953.

Two hundred forty-six children who had positive Mantoux reactions were investigated. A probable source of infection was established for 109 of 213 Australian-born children and for 2 of 33 imigrant children. Probable sources were established for two-thirds of the infants with

positive Mantoux and for two-thirds of the children with clinical manifestations other than cervical adenitis. Of 16 cases of tuberculous adenitis, only one could be traced, suggesting that this disease is often due to a bovine type of organism.

Thirteen adults were discovered with previously unsuspected active pulmonary tuberculosis.

McGUIGAN, Evanston, Ill.

BONE TUBERCULOSIS IN CHILDREN. C. VYAGHRESWARUDU, Indian J. Pediat. **20**:162-167 (July) 1953.

In South India it is felt that almost all bone tuberculosis is of the human type. Ten per cent of orthopedic admissions are for tuberculosis. Proper segregation of pulmonary tuberculosis and adequate hospital facilities are an urgent need.

McGUIGAN, Evanston, Ill.

THE MECHANISM AND HYDROCEPHALIC CONDITIONS IN TUBERCULOUS MENINGITIS WITH THE RELATION TO THE LOCAL TREATMENT WITH STREPTOMYCIN. G. BOI, Ann. ital. pediat. **6**:519 (Dec.) 1953.

The author examines the possibility, frequency, and mechanism of hydrocephalic conditions which may take place during tuberculous meningitis, influenced or not by local streptomycin therapy.

The author assumes that, in the first case, it is somewhat easier to see an increase in spinal fluid which may lead to the hydrocephalus and discusses the importance both of the tuberculous factor, chiefly toxic or chronic, and of the direct and indirect streptomycinic factor in the mechanism by excess of production, by blockage, or by default of reabsorption.

FROM THE AUTHOR'S SUMMARY.

TWO CASES OF TUBERCULOUS MENINGITIS CURED BY THE USE OF ISONIAZID EXCLUSIVELY. A. GENTILI and A. PACI, Minerva pediat. **5**:669 (Aug. 31) 1953.

Two children with proved cases of tuberculous meningitis recovered after treatments with isoniazid exclusively. The doses given were 100 mg. daily in seven divided doses by mouth for 220 days with one child and for 150 days with the other child; injections of 10 to 30 mg. of the drug into the cerebrospinal fluid, either by the cisternal or lumbar route, were continued for the same period of time, at first daily, and later, as the child's condition improved, two or three times a week.

HIGGINS, Boston.

HISTOPLASMOSIS, COCCIDIOMYCOSIS, BLASTOMYCOSIS AND MONILIASIS IN PEDIATRIC PRACTICE. ALBERTO FOIS, Riv. clin. pediat. **51**:452 (Dec.) 1953.

A brief review is given of the etiologic factors, pathogenesis, anatomopathological, and clinical picture and therapy of histoplasmosis, coccidiomicosis, blastomicosis and moniliasis.

The importance of localized infections caused by Histoplasma and Coccidioides is emphasized.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF MONILIASIS. ROANO ROSSI, Riv. clin. pediat. **51**:529 (Dec.) 1953.

After having considered the diffusion of Monilia albicans before and after the antibiotic period, a review has been made of various author's opinions on the action of antibiotics in facilitating and spreading Monilia albicans. After a rapid examination of the various local therapies of Monilia albicans and the general therapies of moniliasis, the use of methyl violet intravenously has been tried on rabbits injected with Monilia albicans; this staining prevents the development of disease but only if used in doses toxic to the animal.

FROM THE AUTHOR'S SUMMARY.

ORAL PENICILLIN TREATMENT OF INFANTS WITH CONGENITAL SYPHILIS. RUDOLF WELLER, Monatschr. Kinderh. **101**:266 (May) 1953.

Seventy-five infants up to 5 months of age who had congenital syphilis were treated with oral penicillin. Dosage was 100,000 units per kilogram of body weight per day, divided into eight doses, and was continued for 14 to 15 days. The average hospital stay was 31 days.

Syphilitic skin lesions disappeared within a short period after treatment was instituted, while osseous and intestinal manifestations cleared usually only after patients had left the hospital. Serologic blood tests became negative at the average of three and one-half months after onset of treatment and remained negative for three and one-half years in the cases followed for the longest period. No Herxheimer reaction or other serious complications of penicillin treatment was detected. Pronouncement of a definite cure should be withheld until patients have been followed for a longer time than in this study. Mortality was 7.5%, as compared to 40% with regimens of older antisyphilitic drugs.

HARTENSTEIN, Syracuse, N. Y.

THE BCG STRAIN AND COMPLICATIONS AFTER BCG VACCINATION. A. C. BRANDWIJK and R. GISPEN, Nederl. tijdschr. geneesk. **97**:336 (Feb. 7) 1953.

The frequency of complications after BCG vaccination in newborn babies which occurred in the Netherlands attracted attention. The complications consisted of lymph node abscesses, and when the vaccine was given orally, otitis media was seen. The vaccine was a Danish strain, cultured according to the method used in the Institut Pasteur in Paris. As comparison of the results of workers in different countries is very difficult, and as a standardization of the BCG vaccine is not yet possible, it will be necessary for each worker to observe the action of the vaccine in the human body continuously for complications and allergic reactions.

VAN CREVELD, Amsterdam.

Diseases of Blood, Heart and Blood Vessels, and Spleen

A SACCULAR OUTPOUCHING OF THE RIGHT VENTRICLE IN A CHILD, VISUALIZED BY ANGIOCARDIOGRAPHY. G. MILLER, M. LOWENTHAL, S. KRAUSE, and P. ROSENBLUM, Am. J. Roentgenol. **69**:69 (Jan.) 1953.

This is the report of a case of a small saccular outpouching of the right ventricle seen by angiocardiography in a 12-year-old boy. The outpouching was thought to be either a congenital diverticulum or a small acquired saccular aneurysm of the right ventricle. No diverticulum has been previously reported in the right ventricle. No contributing disease that might be responsible for ventricular anerysm could be found.

HODGSON, Rochester, Minn.

MYOCARDITIS OF UNKNOWN ETIOLOGY (FIEDLER'S?) TREATED WITH ACTH. ROY F. GARRISON and ROBERT C. SWISHER, J. Pediat. **42**:591 (May) 1953.

A 7-year-old boy had idiopathic myocarditis. He was given corticotropin (ACTH) and digitalis. He was apparently cured in the follow-up study, after 16 months.

MACDONALD, Pittsburgh.

THE INCIDENCE AND SIGNIFICANCE OF SYSTOLIC CARDIAC MURMURS IN INFANTS. W. C. TAYLOR, Arch. Dis. Childhood **28**:54 (Feb.) 1953.

In the examination of 1,133 newborn infants, systolic murmurs were detected in 54 (4.8%).

Periodic observation of a selected group of 20 infants with murmurs revealed that in 14 the murmur had disappeared by the age of one year. In three infants, loud systolic murmurs have persisted to the age of 2 years, and a provisional diagnosis of congenital heart disease has been made in each case. Two infants in the group died, and necropsy revealed evidence of congenital heart disease. In a third infant who died there was no evidence of congenital heart disease at necropsy.

KELLY, Milwaukee.

THE HENOCH-SCHONLEIN SYNDROME. M. J. SIMPKISS, Great Ormond St. J. (No. 5) pp. 7-12, June, 1953.

Fifty-one cases seen between 1938 and 1952 are summarized. It is suggested that the high incidence of positive hemolytic streptococcal throat cultures may be significant as a causative agent. Presence of an utricarial rash seemed to be a strong indication of renal complication.

McGUIGAN, Evanston, Ill.

FAMILIAL ELLIPTOCYTOSIS. I. A. B. CATHIE and H. J. COLDSMITH, Great Ormond St. J. (No. 5) pp. 45-53, June, 1953.

A case of familial elliptocytosis is described in which splenectomy was beneficial. Studies on the rest of the family are included. Six members of the family were found to have the disease.

McGUIGAN, Evanston, Ill.

DIAGNOSTIC VALUE OF CATHETERIZATION OF THE HEART IN CONGENITAL HEART DISEASE. ROBERTO SCHIFFRIN and JULIO GUASCH, Rev. chilena pediat. **24**:334 (Sept.) 1953.

The technique of catheterization of the right heart used in this work, based on Cournand's method, is described.

Under the cardiovascular point of view, five different types of congenital cardiopathies are studied in which cardiac catheterization has been made. The curves of intracavitary pressure are analyzed, and the content of O_2 in the blood specimens of the cavities already sounded together with the study of results obtained determine the type of cardiac anomaly.

FROM THE AUTHORS' SUMMARY.

THE DIAGNOSIS OF AORTIC INSUFFICIENCY IN VIVO AND AT AUTOPSY. A. CASTELLANOS and OTTO GARCIA, Arch. med. inf. **22**:183 (July-Sept.) 1953.

A radiological method is presented, applying retrograde aortography in the diagnosis of aortic insufficiency in the cadaver.

The same method was employed by the authors in the diagnosis of aortic insufficiency or incompetency in the subject. The typical images in the study of two patients whose retrograde aortographies were conclusive for their diagnoses are presented.

There are many cases in which the diagnosis of aortic insufficiency is quite difficult, mainly in such cases in which the symptomatology takes the differential diagnosis with a persistency of the ductus arteriosus, or a persistency of the foramen of Panizza, or an interventricular communication complicated by an aortic insufficiency, very difficult. In such cases, a retrograde aortography is absolutely decisive.

FROM THE AUTHORS' SUMMARY.

MODIFICATIONS IN THE METABOLISM OF LIPIDS AND OF PORPHYRINS IN MEDITERRANEAN ANEMIA. E. SCHWARZ-TIENE, G. CORDA, and P. CAREDDU, Minerva pediat. **5**:829 (Oct. 15) 1953.

Both the patients with Cooley's anemia and their parents have deviations from the normal in the lipids of the blood cells and serum. The percentage of phospholipids is higher in the serum but lower in the red blood cells of patients with Cooley's anemia than in normal persons. The percentages in the blood of the parents, who must have an attenuated thalassemia, are intermediate between those found in the patients and those in normal persons. Similar changes, but not so striking, have been found in the amount of cholesterol, fatty acids, and neutral fats present in the blood cells and sera.

No definite deviation from the normal was found in the amounts of porphyrin in the red cells or in the coproporphyrin excretion in the urine of patients with Cooley's anemia. The impaired hemogenesis is apparently due to the abnormal structure and the reduced enzymatic processes in the red cells, which prevent the linkage of the porphyrin to the iron and not to an impaired synthesis of porphyrin.

The deviation from normal of the blood lipids is apparently a genetic metabolic condition, existing in both thalassemia major and minor.

HIGGINS, Boston.

ANEMIA OF FANCONI. G. SANSONE and M. CRISALLI, Minerva pediat. **5**:971 (Nov. 15) 1953.

Fanconi's syndrome of anemia is a hypoplastic anemia of children, frequently familial in type, characterized by pancytopenia, progressive bone marrow insufficiency, and multiple malformations. The authors describe the previously published cases and then two cases of their own, the first described in the Italian literature. Each of the two boys, both 6 years of age, had the appearance and symptoms of severe anemia, marked cachexia, and frequent nosebleeds; in neither was there a family history of previous blood dyscrasias. The malformations were mainly skeletal, one of the boys having bones absent in one thumb, no right radius, and deformity of both forearms. The other boy had stunted growth, microcephaly, many abnormalities of bone structure, as well as only one kidney, hydronephrosis, and megaloureter.

HIGGINS, Boston.

THE CIRCULATING EOSINOPHILE. G. BARTOLOZZI, S. BORGHERESI, and M. MINUCCI, Riv. clin. pediat. **51**:406 (Nov.) 1953.

After a revision of modern literature upon behavior and clinical signification of peripheral eosinophile cells, the authors made a study of 176 healthy children 0 to 6 years old. On the basis of the obtained data, the average value for eosinophile cells was found to be 246 per cubic millimeter.

FROM THE AUTHORS' SUMMARY.

TRANSITION OF RETOTHELSARCOMA INTO GENERALIZED LEUKEMIC RETICULOSIS IN A CHILD. O. HRODEK and J. JANELE, Pediat. listy **8**:337, 1953.

A case of tumoriform terminal leukemic reticulosis in a 6-year-old girl is described in which the first manifestation was retothelsarcoma of the skin of the leg. In the further course, the process became generalized, the skin being maximally affected. Death occurred a year after the first clinical examination and almost two years after the first appearance of the disease.

A brief outline on views on retothelsarcoma, reticuloses, and their relationship to the other hemoblastoses is included.

FROM THE AUTHORS' SUMMARY.

Diseases of Nose, Throat, and Ear

SURGICAL MANAGEMENT OF ANGIOFIBROMA OF NASOPHARYNX. ARNOLD J. KREMEN, Ann. Surg. **138**:672-677 (Oct.) 1953.

Angiofibromas of the nasopharynx distinctly occur in young pubescent boys, producing a symptom pattern of nasal obstruction, voice and hearing changes, and dangerous bleeding. The lesion grows progressively during the period of adolescence, but after maturity the tumor often regresses. The lesions do not exhibit the classic histological features of malignant neoplasms, but not infrequently they display the characteristics of a positional malignancy where progressive growth of the tumor expands the narrow confines of the nasopharynx, and the threat of repeated exsanguinating hemorrhage endangers the life of the patient.

A technique is presented for surgical management of angiofibromas of the nasopharynx by lateral nasopharyngostomy.

BANTIN, Omaha.

A COMPARATIVE STUDY OF METHODS OF ESTIMATING THE SEVERITY OF STUTTERING. REX V. NAYLOR, J. Speech & Hearing Disorders **18**:30 (March) 1953.

Twenty-four male stutterers, ranging in age from 16 to 35, were graduate students judged for severity of stuttering. The judgments agreed consistently with the stutterers' estimates of severity in the situation, but not with estimates of the severity of stuttering for the preceding several months. Study of the stutterers' experiences in speaking for a test of attitudes toward situations requiring speech yields results consistent with the stutterers' own estimates of severity. Reading six passages with 0.18 seconds of side-tone delay, there was a statistically significant negative relationship to the judges' rating of severity.

PALMER, Wichita, Kan.

VASCULAR RING: A CAUSE OF CONGENITAL STRIDOR. RICHARD W. SMITHELLS, Arch. Dis. Childhood **28**:204-208 (June) 1953.

The causes of congenital stridor are considered, and the suggestion is made that tracheal compression by vascular rings arising from congenital anomalies of the great vessels may not be as uncommon as hitherto supposed.

A case is described in which severe symptoms of tracheal and esophageal compression due to a bilateral aortic arch were dramatically relieved by operation.

KELLY, Milwaukee.

THE INFANT WITH STRIDOR. JOHN APLEY, Arch. Dis. Childhood **28**:423-435 (Dec.) 1953.

Observations are recorded on 80 cases with stridor developing in early infancy. To determine the natural history of the condition, progress was assessed clinically and by ancillary methods for periods up to several years. Attention was directed not only to the sequence of any changes in the larynx but also to general physical and mental development.

Stridor occurred in 11 of 14 siblings in five families. In the whole series, there was a male preponderance in the ratio of five boys to three girls. The average birth weight of boys with stridor was significantly higher than that of girls with stridor and than that of unselected infants of either sex.

In seven cases a congenital cardiac malformation was present, though in only one was it the cause of stridor. Three patients in the series were Mongols; 16 others were mentally retarded.

Feeding difficulties occurred in half the total number. Pulmonary complications were frequent. Chest deformities developed in many cases but were almost invariably transient.

Eleven patients died, and in 10 necropsy was performed. Apart from two cases of meningomyelocoele and one of thyroid enlargment, death was invariably due to pulmonary infection.

In the largest group of cases, stridor was produced by an anatomical anomaly which impaired the patency of the upper respiratory tract; in the majority of these the anomaly was epiglotic. In a second group, stridor was considered to be due to dysfunction of the nervous system. In a third group, stridor originated with an upper respiratory infection.

The mechanism of production of stridor in these groups is discussed, with particular reference to primary and secondary changes in the larynx. It is emphasized that in the investigation of infantile stridor it is essential to make early and repeated observations not only of the larynx and respiratory tract, but of the patient as a whole.

KELLY, Milwaukee.

INFLAMMATIONS OF THE MIDDLE EAR CAUSED BY CANDIDA ALBICANS. K. TOMIĆ-KAROVIĆ and V. POPADIĆ, Schweiz. med. Wchnschr. **83**:59 (Jan. 17) 1953.

From material obtained on antrotomy and mastoidectomy in a 49-year-old farmer, Candida albicans was isolated. It was also isolated from the pus of the middle ear of an 8-year-old girl. This case cleared under treatment with 3% boric acid. The authors could not find any report of inflammation of the middle ear caused by this micro-organism.

AMBERG, Rochester, Minn.

DISEASES OF THE PARANASAL SINUSES IN CHILDHOOD. L. RUEDI, Schweiz. med. Wchnschr. **83**:1247 (Dec. 26) 1953.

The review deals briefly with ethmoiditis acuta necroticans (scarlet fever), Kartagener's syndrome, and the combination of bronchiectasis with chronic sinusitis with the familial fibrosis of the pancreas. Special attention is directed to the so-called occult silent sinusitis which is localized preponderantly in the maxillary sinuses. It is noted that the sinusitis is rather rarely "silent." The diagnosis is established by roentgen examinations, and routine examinations are recommended. Treatment is discussed.

AMBERG, Rochester, Minn.

SOME CASES OF ACUTE OBSTRUCTIVE LARYNGOTRACHEAL BRONCHITIS. D. GOTTI, Clin. pediat. **35**:407 (June) 1953.

Nine children, 5 to 11 years old, from the same neighborhood in Bologna, developed over a period of five days acute laryngotracheobronchitis. One of the patients, a 9-year-old hypogenital

and hyperthymic boy, died; an autopsy was done. In none of the cases could a definite bacterial causative agent be established. It is quite likely that filtrable virus may have been responsible for the infections.

HIGGINS, Boston.

THE TREATMENT OF DIPHTHEROID RHINITIS IN CHILDREN BY THE LOCAL APPLICATION OF FIBRINOLYTIC ENZYMES. E. CHELI, Clin. pediat. **35**:667 (Sept.) 1953.

Diphtheroid rhinitis is defined as the persistent crusty bloody fibrinoid exudate or the impetiginous crusting in and around the nasal cavity; it usually is a sequella of the common cold. Successful results are reported by the local application by a cotton pledget of a solution containing fibrinolytic enzymes, followed by similar application of an antibiotic. The fibrinolytic enzymes are of pancreatic origin, and are sold under the proprietary name, Fibrinoclasi.

HIGGINS, Boston.

TREATMENT OF JUVENILE FIBROMA OF THE NOSE AND THROAT. F. DREFCI, Wien. klin. Wchnschr. **65**:76 (Jan. 16) 1953.

Two boys, 13 and 10 years of age, were submitted to transmaxillary removal of a fibroma of the nasopharynx. This method is regarded as the procedure of choice.

AMBERG, Rochester, Minn.

CHANGES IN BACTERIAL FLORA OF THE THROAT DURING STREPTOMYCIN THERAPY. WALTER GOETERS, Monatsschr. Kinderh. **101**:505-510 (Dec.) 1953.

One hundred thirty-seven children of all age groups received intramuscular streptomycin in doses of 0.5 to 1 gm.; 8 infants received a total of 3 gm. of oral streptomycin. Throat cultures revealed streptomycin-resistant micro-organisms which composed 10 to 20% of the bacterial flora. The persistence of streptomycin-resistant organisms was proved, furthermore, by their growth on culture media containing 200 mg. of streptomycin per cubic centimeter. The percentage of resistant strains bore no relationship to the age of the patient but was dependent on the amount of the drug received by the patient.

The first appearance of streptomycin-resistant organisms occurred on the 15th day of treatment with doses of 0.5 gm., on the 10th day with 0.75 gm., on the 2d day with 1 gm., and with oral administration to young infants. Resistant organisms consisted of strains normally present in throat cultures. Monilia and Candida were prevalent.

Organisms dependent on streptomycin for growth were found in 64 patients when maximal dosage of the drug was used; they were also found in two nurses caring for the infants receiving oral streptomycin. In 5% of attending personnel (physicians, laboratory workers, teachers, and ward and clerical help), in 10% of untreated roommates of patients, and in 31% of nurses streptomycin-resistant strains were found.

Streptomycin-resistant strains had disappeared by 8 to 10 days after cessation of intramuscular therapy and in 3 to 4 weeks after oral treatment.

Comparable results were obtained in mouse experiments.

HARTENSTEIN, Syracuse, N. Y.

STENOSIS OF THE LARYNX IN INFANCY: HAEMANGIOMA OF THE LARYNX. O. B. RAMSE, Acta pædiat. **42**:65 (Jan.) 1953.

A 3-month-old girl suffered from difficulty in inspiration from birth. Attacks of dyspnea set in gradually, with stridor, cyanosis, and loss of consciousness. There were repeated remissions. Direct laryngoscopy revealed a bluish-black swelling in the region of the subglottis, and a postmortem examination showed a hemangioma in the larynx, with hemorrhage, tracheobronchitis, and atelectasis of the lungs. In connection with this case, a brief account is given of the symptomatology, diagnostic possibilities, and treatment of hemangioma in the larynx.

FROM THE AUTHOR'S SUMMARY.

Diseases of Lungs, Pleura, and Mediastinum

NEW TECHNIQUE OF HUMIDIFICATION IN PEDIATRICS. SAMUEL F. RAVENEL, J. A. M. A. **151**:707 (Feb. 28) 1953.

"Alevaire," a detergent, will reduce viscosity by 10% to 24% as measured by an Ostwald viscosimeter. When nebulized in an oxygen tent, "croupette," or incubator it has been found very valuable clinically in treating those pulmonary conditions in which the secretions thicken, such as asthma, bronchiolitis, and pneumonia with atelectasis and after bronchoscopy or tracheotomy, bulbar poliomyelitis, pertussis, kerosene poisoning, and neonatal asphyxia. After experience of one year, the author believes that the use of Alevaire considerably reduced premature and neonatal mortality by decreasing the viscosity of the respiratory secretions.

KIMBALL, Evanston, Ill.

MEDIASTINAL LYMPHOSARCOMA IN AN INFANT. M. H. STICH, J. RUBINSTEIN, A. B. FRIEDMAN, and M. MORRISON, J. Pediat. **42**:235 (Feb.) 1953.

The authors report a case of primary mediastinal lymphosarcoma in a 7-month-old infant who was apparently cured 12 years after x-ray therapy. The original diagnosis was confirmed by needle biopsy.

MACDONALD, Pittsburgh.

A CASE OF TENSION PNEUMOTHORAX COMPLICATING STAPHYLOCOCCAL PNEUMONIA AND EMPYEMA THORACIS. R. SPENCER, Arch. Dis. Childhood **28**:47-48 (Feb.) 1953.

A case of tension pneumothorax and empyema following primary staphylococcal pneumonia has been described.

It is pointed out that in cases of staphylococcal empyema it should be borne in mind that lung abscess, tension cyst, or tension pneumothorax is a distinct possibility. This helps in making an early diagnosis.

Treatment of the tension pneumothorax is described, making use of the Lillingston and Pearson artificial pneumothorax apparatus.

KELLY, Milwaukee.

THE MANAGEMENT OF ASTHMA IN CHILDHOOD. C. T. PIPER, Clin. Rep. Adelaide Child. Hosp. **2**:152-155 (May-Nov.) 1953.

This article is a pamphlet given by the author to the parents of asthmatic children in his practice. In it he explains in simple terms what asthma is, its cause and management. Stress is laid upon "habit asthma," or nervous asthma, and the statement is made that if the development of habit or nervous asthma is prevented, the child has a very good chance of growing out of his disease.

MCGUIGAN, Evanston, Ill.

FOREIGN BODIES IN THE TRACHEA AND BRONCHI. D. ADLER and D. FULLER, South African M. J. **27**:1155-1159 (Dec.) 1953.

The authors reviewed 100 cases of foreign bodies in the trachea or bronchi in children.

Pathology, diagnosis, and symptoms are reviewed. Physical signs and radiologic findings are stressed. Regarding radiology, the need for expiration films is emphasized, and the physician is cautioned against depending too much on radiological findings. If the history is sufficiently suggestive, bronchoscopy should be performed.

Technique of operation is described and postoperative care outlined.

MCGUIGAN, Evanston, Ill.

PNEUMATOCELE IN ACUTE LUNG PATHOLOGY IN CHILDREN. L. PARENZAN, Minerva pediat. **5**:79 (Feb. 15) 1953.

Eighteen and seven days after two children, 3 months and 3 years of age, had recovered from attacks of bronchopneumonia, each child had a recurrence of fever and coughing; the high temperature and fever were of short duration, but x-ray examination revealed in the first child,

one, and in the second child, two, bright circular shadows, apparently emphysematous blebs (pneumatoceles). In one child, the pneumatocele was in the lobe, which had been the seat of the previous pneumonia. The shadows had disappeared when the x-ray examinations were repeated about two weeks later.

HIGGINS, Boston.

CLINICAL CONSIDERATIONS REGARDING PULMONARY SUPPURATION IN CHILDREN. GOMIRATO-SANDRUCCI, Minerva pediat. **5**:906 (Oct. 31) 1953.

After a review of three cases of pulmonary suppuration, the following conclusions were drawn:

1. Pulmonary suppuration is not rare in children and may occur even in the early months of life.

2. Malformations of the bronchi and of the lungs, especially bronchiectasis and cysts, predispose to suppuration.

3. Aerosol therapy is the method of choice, as it permits both the local and the systemic action of the drug.

4. Early diagnosis may be difficult.

5. Correct treatment will depend on knowing the bacterial agent and its sensitivity to various antibiotics and sulfonamide drugs.

6. Correct treatment will usually result in complete cure without surgical intervention, but surgery may be advisable to correct existing malformations.

HIGGINS, Boston.

INTERSTITIAL PNEUMONIA. H. ZELADA, A. WINTER, A. VARGAS, R. MATTE, and S. IBANEZ, Rev. chilena pediat. **24**:340 (Sept.) 1953.

The authors review the clinical picture of interstitial pneumonia based on four cases, three of infants and one in an older child, anatomopathologically checked, and whose most important clinical characteristics were severe involvement of the general status, dyspnea, cyanosis, cough, signs of emphysema, and lack or scarcity of condensation signs. In the infants, a stationary weight curve, diarrhea, and anorexia were also found. In all our cases, the evolution was of the chronic type, its characteristic being a lack of high temperature.

Anatomopathologically, there was found interstitial infiltration mostly of mononuclear elements, lesion of the bronchial epithelium, which was found to be full of a mucoid exudate, and a hyaline membrane which covered the alveolae. In all our cases, hypertrophy of the right heart was found due to difficult hematosis.

FROM THE AUTHORS' SUMMARY.

INSTRUMENTAL EQUIPMENT USED IN TRANSVERSE PLANIGRAPHY. G. C. F. BRINKBOK, H. E. A. FERMIN, and E. J. RENAUD, Maandschr. kindergeneesk. **21**:389 (Dec.) 1953.

A short account is given of the instrumental equipment used in transverse planigraphy. The way in which points situated in and outside the plane of adjustment are sharply depicted or blurred respectively is explained. A description is given of some transverse planigrams of the thorax of five small patients.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF BRONCHIAL ASTHMA WITH CORTICOTROPIN (ACTH). W. J. QUARLES VAN UFFORD, Nederl. tijdschr. geneesk. **97**:140 (Jan. 17) 1953.

Good results of corticotropin (ACTH) therapy in some acute and chronic forms of bronchial asthma are described; other forms of treatment had failed. Corticotropin was given intravenously for five to nine days, sometimes followed by a maintenance dose of one infusion per week. The results are independent from the result of the Thorn test.

VAN CREVELD, Amsterdam.

PSYCHOSOMATIC ASPECTS OF BRONCHIAL ASTHMA. J. GROEN, Nederl. tijdschr. geneesk. **97**:1946 (July 25) 1953.

Clinical observation, personality, and psychologic examination and therapeutic experiences point to a psychogenic cause of bronchial asthma. Psychotherapy partly given as group therapy and often supported by small doses of corticotropin (ACTH), which also has an influence on mental behavior, gave encouraging results.

VAN CREVELD, Amsterdam.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

INFANTILE HYPERTROPHIC PYLORIC STENOSIS RECURRING AFTER RAMMSTEDT'S OPERATION. N. K. MACRAE-GIBSON and B. L. COLES, Arch. Dis. Childhood **28**:130-133 (April) 1953.

Two cases of pyloric stenosis recurring after Rammstedt's operation are reported. In each case a further recurrence occurred after a second operation. Both cases eventually responded to medical treatment.

The literature is reviewed, and the likely causes of relapse are discussed.

It is suggested that true recurrence may be due to an abnormal tendency of the pyloric fibers to proliferate.

KELLY, Milwaukee.

RECURRENT PAROTITIS IN CHILDREN. H. EVERLEY JONES, Arch. Dis. Childhood **28**:182-186 (June) 1953.

Seventeen cases of recurrent swelling of the parotid gland are described.

The condition is thought to be due to infection originating in the mouth or postnasal space ascending to the parotid duct, associated with stagnation of the secretion in the gland.

Treatment consists in simple massage of the gland towards Stensen's duct, and the injection daily of 1 ml. of penicillin (100,000 units) slowly into Stensen's duct daily for six days.

KELLY, Milwaukee.

News and Comment

GENERAL NEWS

Specialists Certified by The American Board of Pediatrics, Inc.—The following physicians were certified as specialists by The American Board of Pediatrics, Inc., in San Francisco, on June 25, 26, and 27, 1954.

Albis, Michael D., Riverside, Calif.
Amer, Julius, Denver.
Anderson, Richard L., San Francisco.
Aronson, Lawrence, San Rafael, Calif.
Austin, R. Lee, Fullerton, Calif.
Balken, John Bruce, Ogden, Utah.
Ball, Walter Owen, San Anselmo, Calif.
Bauer, Edward G., Walnut Creek, Calif.
Berryhill, M. Boyd, Eugene, Ore.
Bigler, Muriel Seaver, San Francisco.
Bishop, John S., San Diego, Calif.
Blair, William Campbell, Berkeley, Calif.
Bramham, James C., Jr., Sacramento, Calif.
Bramson, Morton Ben-Ari, Albuquerque, N. Mex.
Burnip, S. Robert, San Francisco.
Byrne, Basil K., El Paso, Texas.
Caffee, James Leslie, Fresno, Calif.
Centeno, Pilar Aquino, Duarte, Calif.
Cochrane, William A., Toronto, Canada.
Cook, Sheldon C., Lafayette, Calif.
Corsa, Leslie, Jr., Mill Valley, Calif.
Cox, Catherine Haney, Mill Valley, Calif.
DeLilly, Mayo Ralph, Los Angeles.
Dennis, James L., Galveston, Texas.
Denton, Robert, Oakland, Calif.
Elliott, Goodwin C., Jr., Redwood City, Calif.
English, Dorothy A., San Rafael, Calif.
Fager, Donald Bruce, Wenatchee, Wash.
Feinstein, Myron Sandford, Redwood City, Calif.
Feldman, Robert, New York.
Fernandez, Gracia F., Manhasset, N. Y.
Folts, Lynd Louis, Corvallis, Ore.
Freed, Ivan Graham, Palo Alto, Calif.
Freeman, Murray Taylor, Redlands, Calif.
Fulton, Robert Dalzell, Aberdeen, Wash.
Germain, Ronald O., Cincinnati.
Gillespie, Andrew Erroll, Victoria, B. C., Canada.
Hansen, Elwood Troyer, Los Angeles.
Hanson, Virgil, Riverside, Calif.
Havard, Edward, Menlo Park, Calif.
Hedden, Alan Maxwell, Burlingame, Calif.
Hoeflich, Bert J., Eugene, Ore.
Holtzman, Alan Elliott, Panorama City, Calif.
Hornberger, Ralph C., Stockton, Calif.
Hughes, William Francis, Fort Lewis, Wash.
Hyman, Carol Brach, Los Angeles.
Jensen, Gordon Duff, Bellevue, Wash.
Jessup, Robert Bruce, Menlo Park, Calif.
Johns, Richard B., Phoenix, Ariz.
Johnson, Newell Arnold, Covina, Calif.
Johnson, Robert E., Arcadia, Calif.
Kerr, William J., Jr., San Rafael, Calif.
Kleinmaier, G. Warren, San Francisco.
Knudson, Alfred George, Jr., Pasadena, Calif.
Kraft, Warren John, Wenatchee, Wash.
Lann, Stanley Hall, Burlingame, Calif.
McGovern, Robert Gregory, Edwards, Calif.
McMillan, Ray F., Oakland, Calif.
Margileth, Andrew Menges, Corona, Calif.
Marshall, Bruce H., Sacramento, Calif.
Martelle, Robert Raymond, Corona, Calif.
Meisenheimer, W. E., Rosemead, Calif.
Miller, Alvin Peter, Denver.
Mintz, A. Aaron, San Pedro, Calif.
Mostofi, Abol Ghassem, Chicago.
Murphy, Robert E., Omaha.
Nelson, Russell Alan, Atwater, Calif.
Patterson, H. Eugene, Yakima, Wash.
Philips, Irving, New York.
Pickering, Donald E., San Francisco.
Polson, A. Borden, Los Angeles.
Pulford, Gurdon Saltonstall, Palo Alto, Calif.
Rapaport, Robert J., Oakland, Calif.
Reade, Carleton Wight, Jr., Olympia, Wash.
Richards, John Clarence, Los Altos, Calif.
Rogerson, Alexander G., Berkeley, Calif.
Rostel, George P., Palo Alto, Calif.

Rowe, Robert T., Nellis Air Force Base, Nev.
Rubell, Earl B., Sherman Oaks, Calif.
Ruhstaller, Frank David, Stockton, Calif.
Santiago, Pura Dizon, San Antonio, Texas.
Schaeffer, Robert H., Walla Walla, Wash.
Schoen, Edgar J., Oakland, Calif.
Senz, Edward Henry, San Francisco.
Sexton, Harold Miller, Honolulu, T. H.
Siegel, Earl, Hamilton Air Force Base, Calif.
Simon, Henry, Montrose, Calif.
Stork, Robert Mulkey, La Jolla, Calif.
Strauss, J. F., Portuguese Bend, Calif.
Terry, Robert T., San Francisco.
Turbeville, Louis R., Dallas, Texas.
Waite, Charles Loring, Pearl Harbor, T. H.
Ward, Donald Owen, Bremerton, Wash.
Warmington, William J., Seattle.
Weill, Charles C., Daly City, Calif.
Weiss, Robert C., Los Angeles.
Williams, Byron K., Sherman Oaks, Calif.
Wright, Phyllis Mann, Torrance, Calif.
Yaeger, John J., Pueblo, Colo.

A special certificate for noncitizens was given to P. Govinda Menon, Baltimore.

Pediatricians Certified in Pediatric Allergy.—The following pediatricians have been certified in the subspecialty of Pediatric Allergy at the examination held in Rochester, N. Y., on May 9, 1954.

Cagan, Maclyn, Newark, N. J.
Collins-Williams, Cecil, Toronto, Ontario, Canada.
Johnstone, Douglas Edward, Rochester, N. Y.
Lubens, Herman, Fair Lawn, N. J.
Martoccio, Rocco J., Utica, N. Y.
Rosenblum, Arthur H., Chicago.
Speer, Frederic, Kansas City, Kans.

Joint Session of Chicago Pediatric and Chicago Medical Societies.—The meeting of the Chicago Pediatric Society in a joint session with the Chicago Medical Society, on Feb. 16, 1954, was a Memorial Meeting to Dr. Louis S. Robins.

ANNOUNCEMENTS

Annual Meeting of American Academy for Cerebral Palsy.—The Eighth Annual Meeting of the American Academy for Cerebral Palsy will be held on Nov. 4, 5, and 6, 1954, in Williamsburg, Va., at the Williamsburg Inn.

Pediatric Fellowship.—Memorial Center for Cancer and Allied Diseases announces the establishment of a second Fellowship in Pediatric Oncology. The pediatric residencies held under these fellowships are approved for partial credit by the American Board of Pediatrics. Appointments are made July 1 and January 1, for 6 or 12 months. The 30-bed pediatric service is exclusively for the study and treatment of children with cancer and related diseases. The salary is $3,600 annually, plus maintenance. For further information, communicate with Director, Pediatric Service, Memorial Center, 444 East 68th St., New York 21.

Sixth Annual Morris Lamm Blatt Memorial Fund Lecture.—The pediatric staff of the Cook County Hospital announces that the Sixth Annual Morris Lamm Blatt Memorial Fund lecture will be given Monday, Oct. 18, 1954. Dr. Otto Glasser, Chairman of the Department of Biophysics of the Cleveland Clinic, will speak on "Medical Physics and the Neoatomic Age." The lecture will be presented at 8:30 p.m. in the medical amphitheatre of the Cook County Hospital.

Fellowships in Management of Poliomyelitis.—The National Foundation for Infantile Paralysis is granting clinical fellowships in the management of poliomyelitis. Applications should be sent to the Division of Professional Education, National Foundation for Infantile Paralysis, 120 Broadway, New York 5, either before Sept. 1, 1954, or Dec. 1, 1954.

Postgraduate Course in Pediatric Allergy.—A postgraduate course in Pediatric Allergy will be given at the New York Medical College, Flower and Fifth Avenue Hosptials, Nov. 3, 1954, to May 25, 1955, under the direction of Dr. Bret Ratner. The course will be on Wednesday, from 9 a. m. to 4 p. m., and the fee is $300. For registration, apply to the office of the Dean, New York Medical College, Fifth Avenue at 106th St., New York 29.

Annual Convention of National Society for Crippled Children and Adults.—The Annual Convention of the National Society for Crippled Children and Adults will be held Nov. 3 to 5, 1954, at the Hotel Statler, Boston.

PERSONAL NEWS

Appointment for Dr. Robert B. Lawson.—Dr. Robert B. Lawson, who has been head of the Department of Pediatrics of the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C., accepted the position of head of the Department of Pediatrics at University of Miami School of Medicine, Miami, Fla.

CORRECTION

Owing to a typographical error on the manuscript as received from the authors, the name of the senior author of the case report, "Rupture of Stomach, Spleen, and Left Hemidiaphragm," on page 616 of the May issue of the JOURNAL was incorrectly spelled. The correct name of this author is Saul Schwartzbach, M.D.

Books

1953-1954 American Pediatric Directory: A Listing of Pediatricians of the United States, Canada and Hawaii with Biographical Information. Edition 6. Edited by Joe T. Smith, M.D. Price, $15. Pp. 275. Joe T. Smith, 3541 Broadway, N.E., Knoxville, Tenn., 1953.

We are in receipt of the new "American Pediatric Directory" for 1953 and 1954. It is a paper-bound volume of about 275 pages. It is very complete and should be most useful.

Advances in Pediatrics. Volume 6. Edited by S. Z. Levine. Price, $7.50. Pp. 273. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1953.

Volume 6 of the popular "Advances In Pediatrics" presents as usual various monographs of contemporary interest to pediatricians. The authors are authorities in their fields, and the present volume is comprised of seven monographs of timely interest.

Topics included are "Lymphosarcoma in Childhood," by Harold Dargeon, "Preventive Prenatal Pediatrics," by Theodore Ingalls, "Intestinal Obstructions in the Neonatal Period," by C. Evrett Koop, "Hemolytic Disease of the Newborn," by Philip Levine and co-workers, "Pulmonary Pathology in the Newborn," by Edith Potter, "The Lypoidoses," by Van Seveld, and "Megaloblastic Anaemia of Infancy," by Zuelzer.

All of these monographs are very well written, comprehensive, and thoroughly up to date. Each in its field offers everything a pediatrician could desire in the way of information. The book is heartily recommended to all pediatricians. It should be read by all and will profit those who do read it.

Child Training and Personality. By John W. M. Whiting and Irvin L. Child. Price, $5. Pp. 353. Yale University Press, 143 Elm St., New Haven 7, Conn., 1953.

This book is a report of a study pertaining principally to the effect which child-training practices have on child personality and the effect that adult personality has on customary responses to illness. The sources of material were taken from ethnographic reports regarding the habits and culture of 75 different primitive societies. Five systems of childhood behavior were dealt with, namely, oral, anal, sexual, dependence, and aggression. Comparisons made betweeen the primitive races and American middle class groups in certain types of behavior indicated that the American group was quite extreme in the severity of toilet training and quite severe in the general socialization of their children. Sex training was studied from four aspects —masturbation, heterosexual play, homosexual play, and immodesty. Reactions to illness was judged to be a reliable index of personality characteristics.

Psychoanalytic theory, according to these authors, indicates that extreme frustration or extreme indulgence of a particular form of behavior in childhood may produce a continuing fixation of interest on that particular form of behavior. The origin of guilt was studied in relation to personality development.

Two conclusions were drawn: (1) that child training the world over is in certain important respects identical; in all societies the infant must be changed into a responsible adult, obeying the rules of his society, and (2) societies differ widely from each other in the precise character of the rules to which the child must be taught to conform.

This volume is in no way a guide book to child training, as the title might suggest. It is, however, an interesting psychoanalytic approach to the study of human behavior in relationship to personality.

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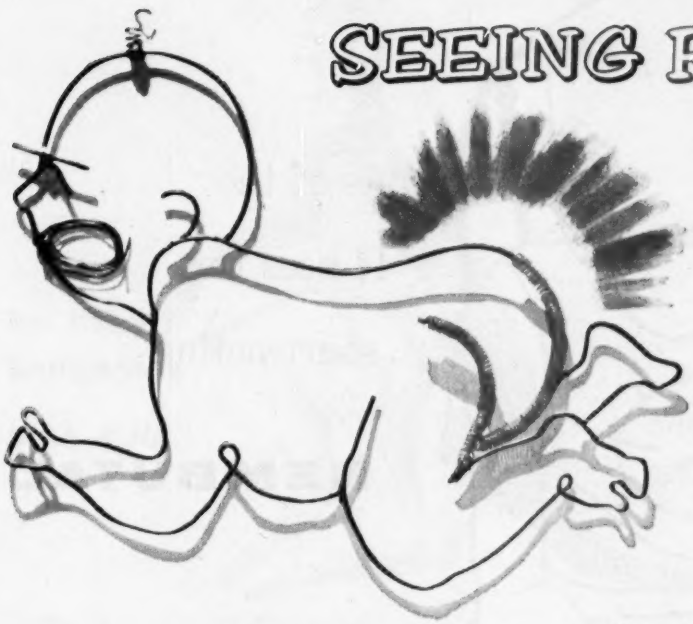

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References: 1. Goldstein, L. S.: Clin. Med. 59: 455, 1952. 2. Pratt, A. G.: A.M.A. Am. J. Dis. Child. 82: 429, 1951.

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Schaerrer, W. C., J. Missouri M. A., 37:287.

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1. Bolliger, A., and Pascoe, J. V.: Australian Journal of Science *15*:215 (June) 1953.
2. Gunther, M.: Brit. J. Nutrition *6* (No. 2): 215, 1952.

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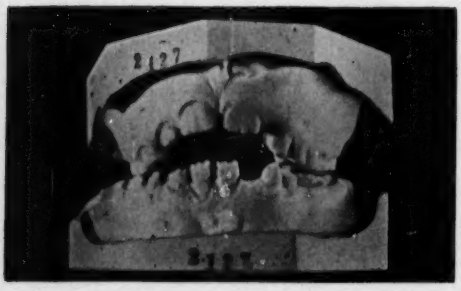

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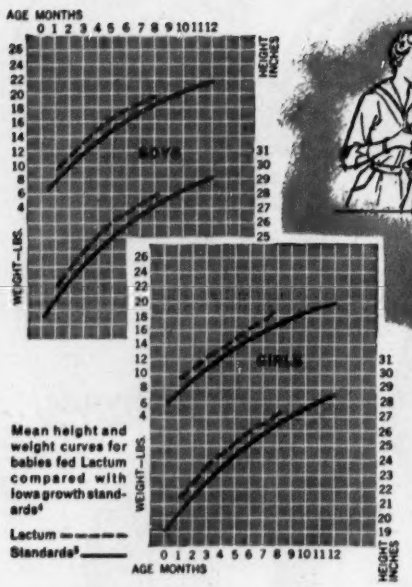
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0 1 2 3 4 5 6 7 8 9 10 11 12
BOYS
GIRLS
WEIGHT—LBS.
HEIGHT INCHES
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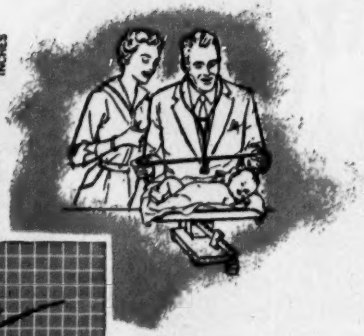
Lactum
Standards[5]



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(1) Jeans, P. C.: In A.M.A. Handbook of Nutrition, Ed. 2, Philadelphia, Blakiston, 1951, p. 275. (2) Albanese, A. A.: Pediat. 8: 455, 1951. (3) Holt, L. E., Jr., and McIntosh, R.: In Holt Pediatrics, Ed. 12, New York, Appleton-Century-Crofts, Inc., 1953, pp. 175-178. (4) Frost, I. H., and Jackson, R. L.: J. Pediat. 39: 589, 1951. (5) Jackson, R. L., and Kelly, H. G.: J. Pediat. 27: 215, 1945.

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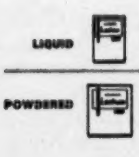

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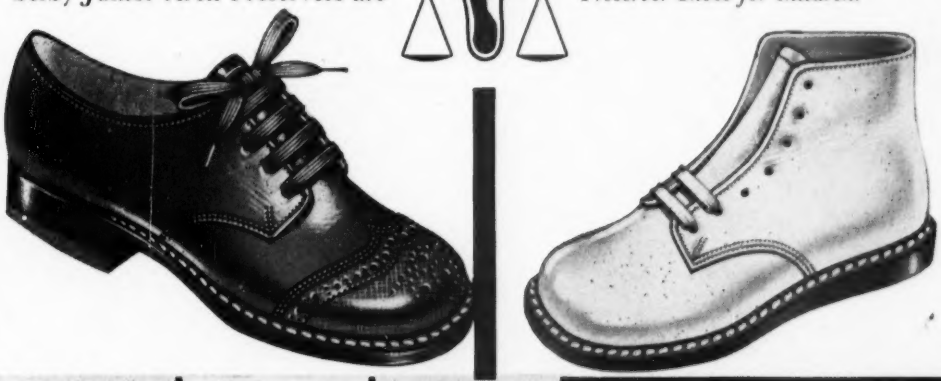

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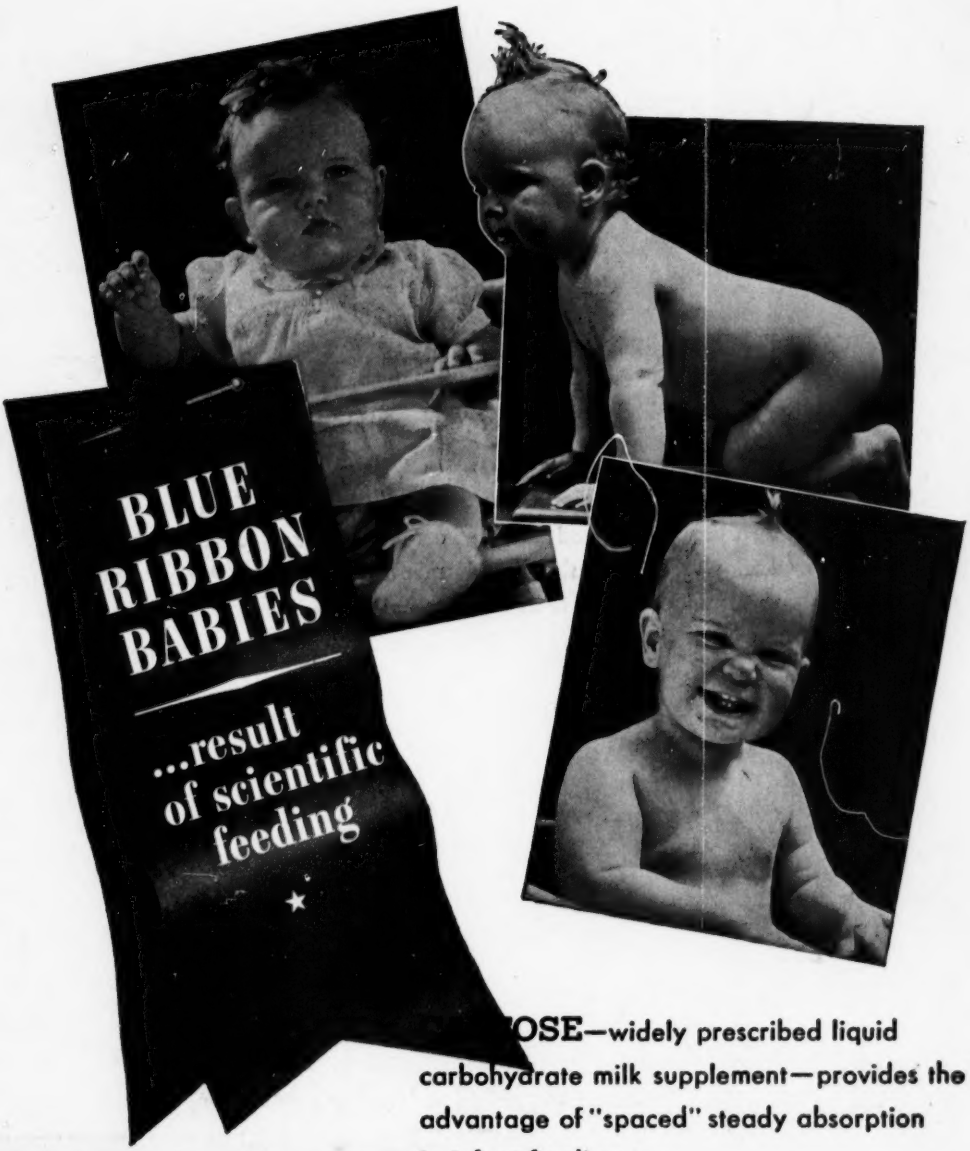

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